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METABOLISM OF PESTICIDES
UPDATE III

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UPDATE III

By Calvin M. Menzie

UNITED STATES DEPARTMENT OF THE INTERIOR
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Appendix II 709

Metabolism of Pesticides

Update III

by

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Division of Ecological Services
Washington, D.C. 20240

This publication supplements its predecessors, Metabolism of Pesticides (1969), Metabolism of Pesticides--An Update (1974), and Metabolism of Pesticides--Update II (1978).

The 1969 and 1974 publications are available through the National Technical Information Service, U.S. Department of Commerce, 5285 Port Royal Road, Springfield, Virginia, 22161. These may be ordered by number:

Metabolism of Pesticides (1969)	PB-300-613
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ABATE (Temephos) [*O,O,O',O'*-Tetramethyl-*O,O'*-thiodi-*p*-phenylene phosphorothioate]

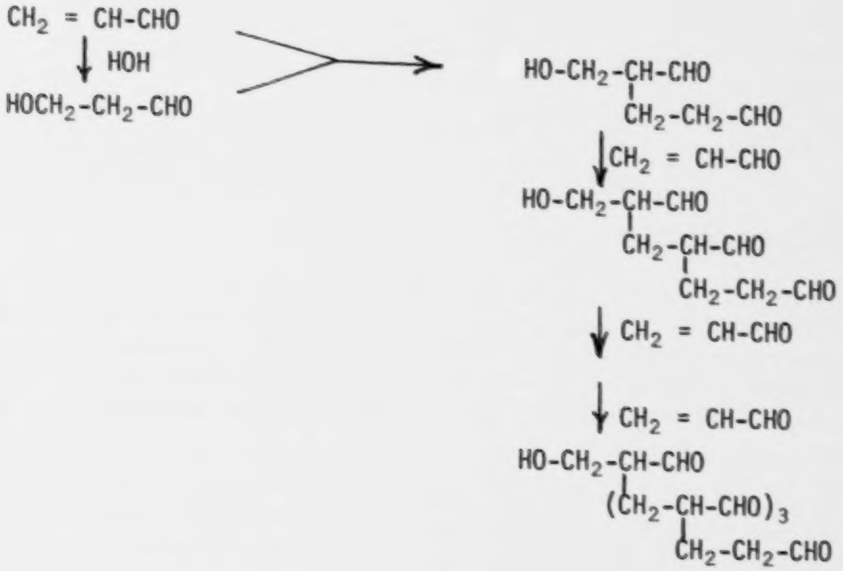
When ^{14}C-ring-labeled abate was sprayed onto lactating goats, most of the radioactivity remained in the hair and hides. Analyses showed the presence of temephos sulfoxide and sulfone in fat; temephos sulfoxide, temephos sulfone, and temephos in liver; 4,4'-thiodiphenol, 4,4'-sulfinyldiphenol, and 4,4'-sulfonyldiphenol, free and conjugated, in urine; and 4,4'-sulfinyldiphenol and temephos sulfoxide in feces (Chiu and Blinn, 1975).

2-Amino-4-phenylthiazole

Following exposure of fish to the anesthetic 2-amino-4-phenylthiazole, the water was analyzed for metabolites. The major biotransformation product, when rainbow trout (*Salmo gairdneri irideus*), carp (*Cyprinus carpio*) or medaka (killifish, *Oryzias latipes*) were used, was identified as 2-amino-4-phenylthiazole-2-*N*-β-mono-D-glucopyranosiduronic acid. A minor metabolite in rainbow trout was identified by UV and IR spectroscopy as 2-acetamido-4-(4'-hydroxyphenyl)thiazole. Chromatography suggested that carp also produced this compound (Shimura and Sekizawa, 1975; Suzuki et al., 1977; Sekizawa et al., 1975).

ACROLEIN (Acrylaldehyde) [2-Propenal]

Degradation of acrolein approximated first-order kinetics. A relatively nonvolatile metabolite, which dissipated rapidly, was observed. A positive reaction was obtained with dinitrophenylhydrazine but the product was not identified (Bowmer and Higgins, 1976). In other studies in acid conditions, the primary reaction was described as a reversible hydrolysis to β-hydroxypropionaldehyde (Pressman and Lucas, 1942). In alkaline conditions (0.0015 to 0.012 N-NaOH), the primary reaction was described as a condensation to a pentamer (Gilbert and Donleavy, 1938).


CH2 = CH-CHO
HOH
HOCH2-CH2-CHO
HO-CH2-CH-CHO
CH2-CH2-CHO
CH2 = CH-CHO
HO-CH2-CH-CHO
CH2-CH-CHO
CH2-CH2-CHO
CH2 = CH-CHO
CH2 = CH-CHO
HO-CH2-CH-CHO
(CH2-CH-CHO)3
CH2-CH2-CHO

AKTON [O-(2-Chloro-1-(2,5-dichlorophenyl)vinyl) O,O-diethyl phosphorothioate]

Akton persisted in Sultan silt loam and followed first-order kinetics. When calculated over a 5-year test period, the calculated half-life was:

2-lb granular treatment, 57.4 weeks;
2-lb spray treatment, 62.1 weeks;
10-lb spray treatment, 84.3 weeks.

(Getzin, 1977)

ALACHLOR [2-Chloro-2',6'-diethyl-N-(methoxymethyl)acetanilide]

The degradation of alachlor by soil fungi was studied. Of eight fungi studied, *Chaetomium globosum* was most active and produced, in addition to inorganic chloride, four metabolites identified as: 2-chloro-2',6'-diethylacetanilide (II); 2,6-diethyl-N-methoxymethylaniline (V); 2,6-diethylaniline (IV); and 1-chloroacetyl-2,3-dihydro-7-ethylindole (III). The other fungi incubated with alachlor for 7 days degraded varying amounts of alachlor:

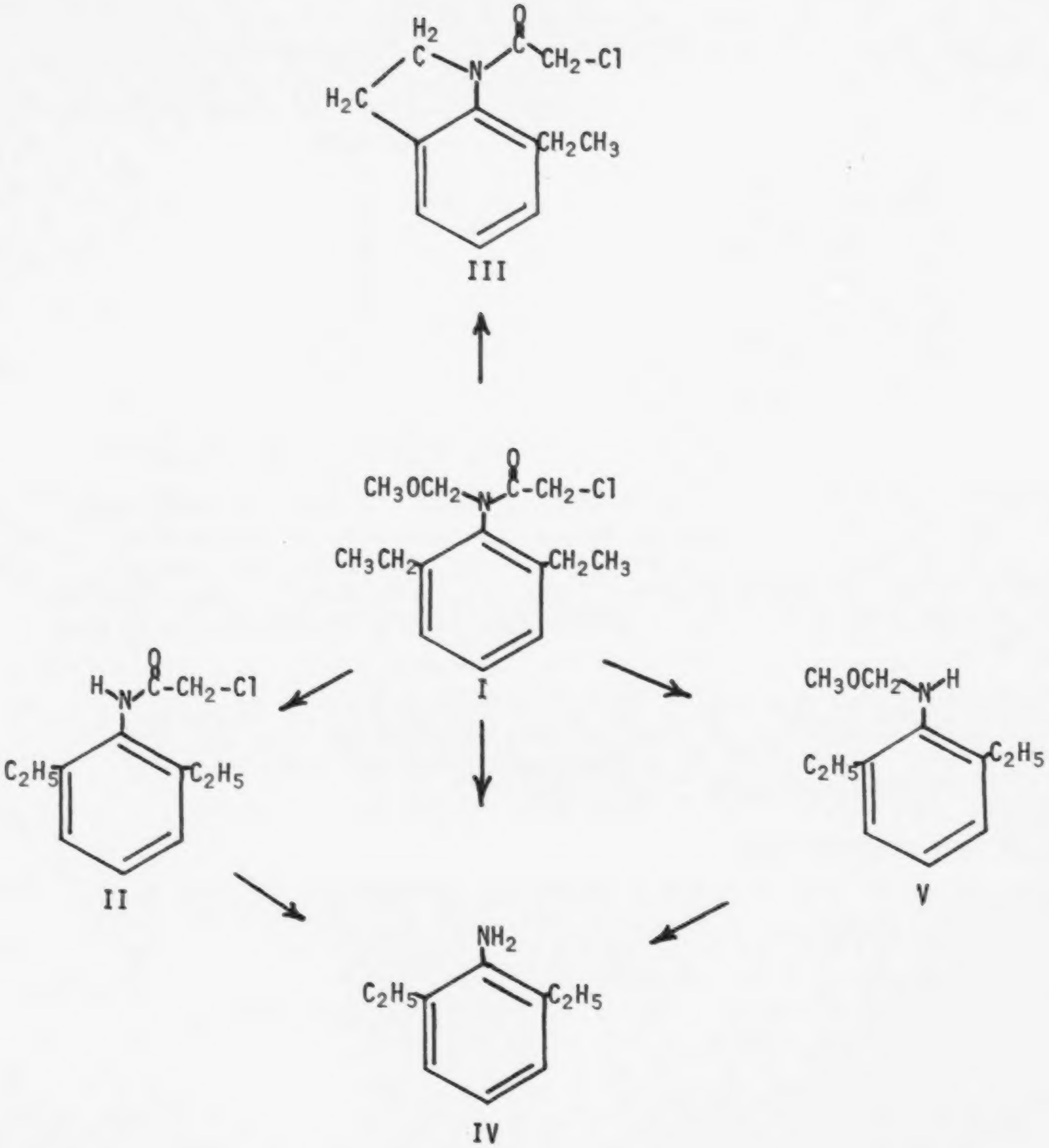
Fungus	% degraded
Penicillium sp.	0
Trichoderma sp.	0
Fusarium roseum	0
Alternaria sp.	4
Phoma sp.	11
Chaetomium bostrychodes	18
Paecilomyces sp.	62
Chaetomium globosum	100

(Tiedje and Hagedorn, 1975)

Ring-^{14}C-labeled alachlor and propachlor were studied in a model ecosystem. Alachlor was degraded into eight compounds and propachlor into seven compounds. None were identified. In each case some of the material was unextractable. There was no evidence of magnification of the two compounds or their metabolites in the food chain (Yu et al., 1975b).

The half-life of alachlor in soils was found to be 7 to 14 days. Four major metabolites of alachlor were observed but only two were identified: 2-chloro-2',6'-diethylacetanilide and 1-chloro-acetyl-2,3-dihydro-7-ethylindole (Chou, 1978).

(See also propachlor.)


H2
C
N
O
C
CH2-Cl
H2C
CH2CH3
III
CH3OCH2
N
O
C-CH2-Cl
CH3CH2
CH2CH3
I
H
N
O
C-CH2-Cl
C2H5
C2H5
II
CH3OCH2
N
H
C2H5
C2H5
V
NH2
C2H5
C2H5
IV

ALDICARB (Temik) [2-Methyl-2-methylthiopropionaldehyde O-methylcarbamoyl oxime]

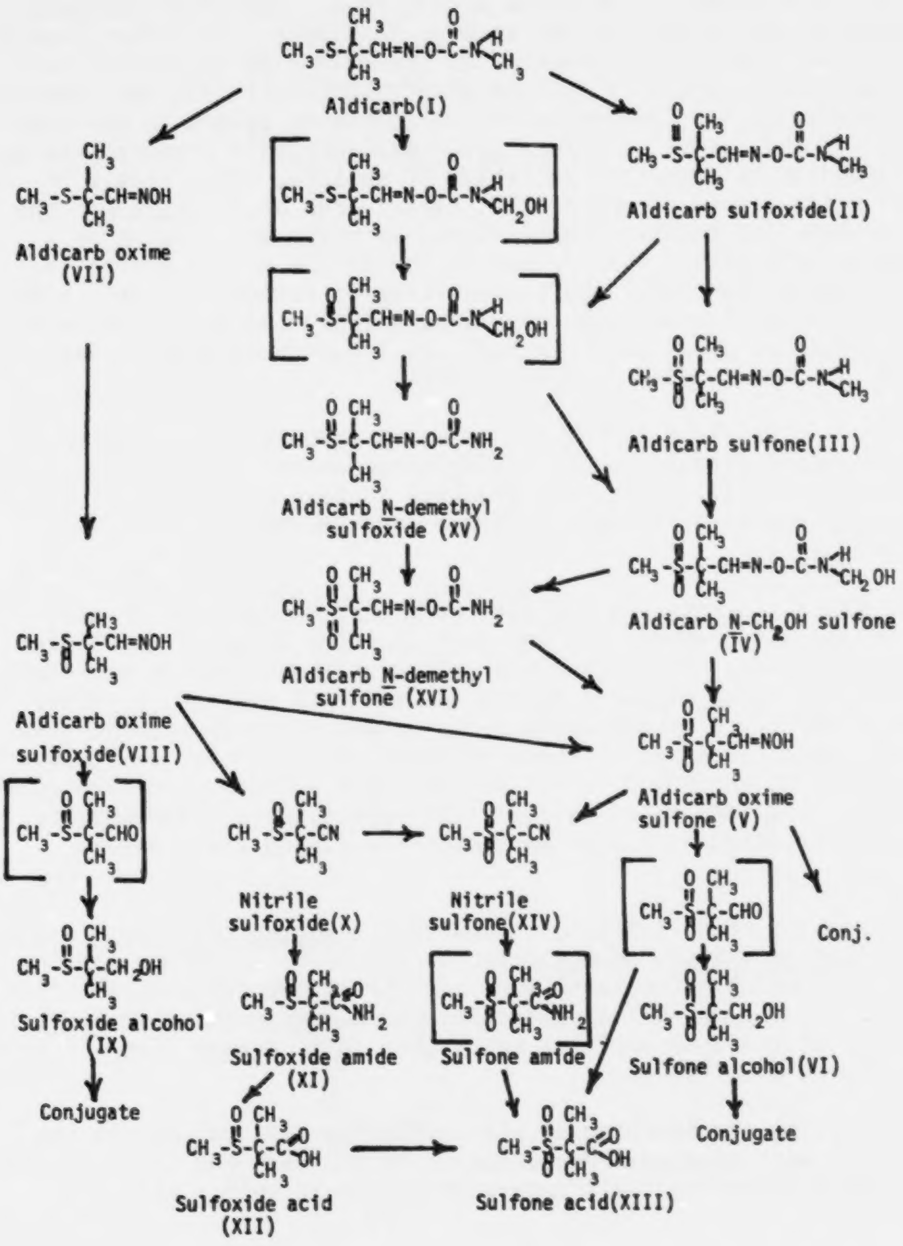
In animals, aldicarb degradation was rapid and 80% of a single oral dose was eliminated in the urine within 24 h. The observed route of degradation was apparently the same as in plants. In cotton leaves, aldicarb was completely converted to the sulfoxide within 4-9 days at moderate temperatures. In potato plants, the half-life was reported as less than 24 h. Conversion of the sulfoxide seemed to be slow. Removal of the methyl carbamoyl group by hydrolysis produced the oxime corresponding to precursor sulfoxide or sulfone. Very little of either oxime seemed to accumulate, either free or conjugated. The main pathway led to the alcohol-sulfoxide which was present as a glycoside primarily. This accounted for 70-80% of the cotton leaf water-soluble fraction. Small quantities of sulfonyl alcohol also formed. In an alternate pathway, some sulfinyl amide was observed. The degradation of aldicarb in soil was found to be qualitatively similar to that in plants (Harvey, 1974).

Aldicarb was oxidized to the sulfoxide by soybean root homogenates. This was found largely in the 25000g supernatant. This activity, on a protein weight basis, was greatest in bean and soybean root 25000g supernatants followed by corn, sorghum, barley and tomato (Kreuger, 1977).

Spider mites (Tetranychus urticae Koch) were exposed to ^{14}C-aldicarb in a metabolism chamber. In addition to eight unidentified radioactive compounds, the recovered organosoluble radioactive material included aldicarb, aldicarb sulfoxide, aldicarb sulfone, aldicarb oxime sulfoxide, aldicarb oxime sulfone, and aldicarb nitrile sulfoxide. When the experiment was repeated with aldicarb sulfoxide, in addition to unchanged sulfoxide, aldicarb sulfone, aldicarb oxime sulfoxide, aldicarb oxime sulfone, aldicarb nitrile sulfoxide and three unidentified compounds were observed (Chang and Knowles, 1978).

Two species of free-living soil nematodes (Aphelenchus avenae and Panagrellus redivivus) were exposed to aldicarb. Although the levels of aldicarb which accumulated were similar in the two species, the rates of uptake, metabolism and elimination were greater in P. redivivus. The level of toxic metabolites was higher in A. avenae after 24 h (Batterby et al., 1977).

The conversion and leaching of aldicarb using soil columns in the laboratory were studied. Measurements of aldicarb and its sulfoxide and sulfone showed that all were very mobile in soil. Aldicarb


Aldicarb(I)
Aldicarb oxime (VII)
Aldicarb sulfoxide(II)
Aldicarb sulfone(III)
Aldicarb N-demethyl sulfoxide (XV)
Aldicarb N-CH2OH sulfone (IV)
Aldicarb N-demethyl sulfone (XVI)
Aldicarb oxime sulfoxide(VIII)
Aldicarb oxime sulfone (V)
Nitrile sulfoxide(X)
Nitrile sulfone(XIV)
Conj.
Sulfoxide alcohol (IX)
Sulfoxide amide (XI)
Sulfone amide
Sulfone alcohol(VI)
Conjugate
Conjugate
Sulfoxide acid (XII)
Sulfone acid(XIII)

conversion followed first-order kinetics with a half-life of about 2 days. The half-life in two soils for the sulfoxide was 12 and 23 days (Leistra et al., 1976).

In other studies, the estimated half-life of aldicarb in Houston black clay was 54 days at 23C and 14 to 20 days at 42C. In Beaumont clay, the half-life was 15 to 28 days at 23C. At 42C, 34% of the aldicarb decomposed in 2 to 4 days and over 70% decomposed in 16 to 18 days (Supak et al., 1977).

Other laboratory studies with sandy loam and five sand soils indicated extensive fragmentation of aldicarb with up to 82% of applied labeled material recovered as $^{14}CO_2$. The sulfoxide and sulfone were the major solvent extractable metabolites. Some of the unextractable label appeared in the humic and fulvic acid soil fractions (Richey et al., 1977).

At 15C, the rate constants for aldicarb conversion in seven soils varied between 0.078 d^{-1} in a peaty sand to 0.35 d^{-1} in a clay loam (Smelt et al., 1978c).

Aldicarb sulfoxide loss from soil followed first-order kinetics. The $t_{1/2}$ at 15C was 20 days in a clay loam and 46 days in a peaty sand. At 15C, 52 to 76% of the sulfoxide was converted to sulfone during the study (Smelt et al., 1978b).

The loss of aldicarb sulfone from soil was variable. While first-order kinetics described the initial loss as 2 to 3 times $t_{1/2}$, after 56 days on clay loam soil or 112 on a greenhouse soil, the degradation rate was faster. At 15C, in plough layer soils, sulfone $t_{1/2}$ ranged from 18 to 154 days in a clay loam and a peaty sand, respectively. In deeper layers, the rate was slower (Smelt et al., 1978a).

When a 10% granular formulation of aldicarb was applied to soil in which potatoes were grown, the aldicarb was not detected in the potatoes at harvest (128-174 days post treatment). Levels of the sulfoxide and sulfone ranged from 0.02 to 0.77 mg (as sulfone)/kg fresh weight potato. Residues were higher in peelings than in peeled potatoes (Smelt et al., 1977a).

In soil, degradation of aldicarb was greater than 10% at 23C in Beaumont soil. About 24% of the added aldicarb was lost from moist soil; 46% from dry soil. IR studies of aldicarb-Al-montmorillonite complexes indicated that degradation was initiated, near strong acid clay surfaces, by protonation of the carbonyl oxygen and possibly the oxime nitrogen (Supak, 1972).

Under field conditions, aldicarb half-life was about 7 days in loam soil. Formation of CO_2 from aldicarb was fairly rapid, indicating extensive degradation (Coppedge et al., 1977).

ALDRIN, DIELDRIN, ISODRIN, and ENDRIN

Aldrin

1,8,9,10,11,11-Hexachloro-2,3-7,6-endo-2,1-7,8-exo-tetracyclo $[6.2.1.1^{3,6}.0^{2,7}]$dodec-4,9-diene

Dieldrin

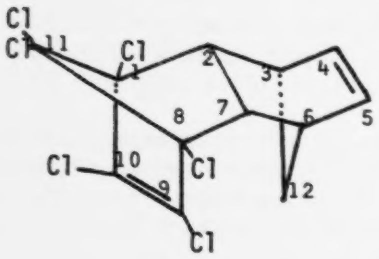
1,8,9,10,11,11-Hexachloro-4,5-exo-epoxy-2,3-7,6-endo-2,1-7,8-exo-tetracyclo$[6.2.1.1^{3,6}.0^{2,7}]$dodec-9-ene

Isodrin

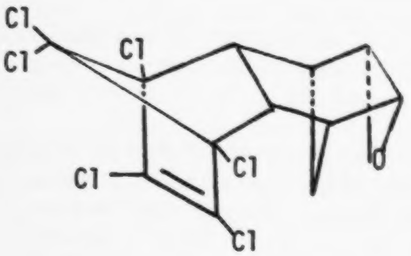
1,8,9,10,11,11-Hexachloro-2,3-7,6-endo-2,1-7,8-endo-tetracyclo $[6.2.1.1^{3,6}.0^{2,7}]$dodec-4,9-diene

Endrin

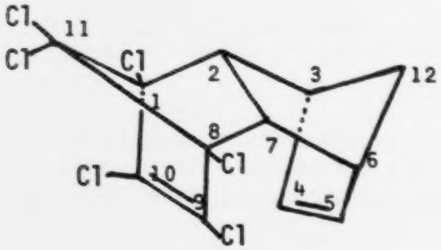
1,8,9,10,11,11-Hexachloro-4,5-exo-epoxy-2,3-7,6-endo-2,1-7,8-endo-tetracyclo$[6.2.1.1^{3,6}.0^{2,7}]$dodec-9-ene


Cl
Cl
11
Cl
1
2
3
4
5
6
7
8
Cl
10
9
Cl
12
Cl

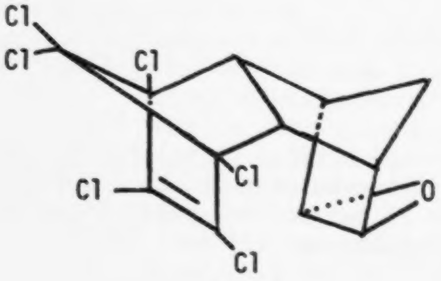
Aldrin


Cl
Cl
Cl
Cl
Cl
Cl
O

Dieldrin


Cl
11
Cl
Cl
2
3
12
1
8
7
Cl
6
Cl
10
4
5
9
Cl

Isodrin


Cl
Cl
Cl
Cl
Cl
O
Cl

Endrin

ALDRIN, DIELDRIN, ISODRIN, ENDRIN

Liver microsomes were prepared from male Sprague-Dawley rats and incubated with aldrin. Analyses indicated conversion of aldrin to dieldrin. Preexposure of rats to phenobarbital increased the microsomal conversion of aldrin to dieldrin (Ghiasuddin and Menzer, 1976).

The comparative metabolism of dieldrin in rats and in mice receiving a single dose of dieldrin was investigated. Differences were primarily quantitative. Fecal metabolites from the CFE rats included 12-hydroxydieldrin; 4,5-trans- and cis-dihydroaldrindiol and aldrin dicarboxylic acid (ADA) (or dihydrochlordenedicarboxylic acid). In the rat urine, there were no metabolites with a polarity greater than ADA. Mouse urine, however, contained a relatively large amount of polar metabolites. Compounds identified in urine included 12-hydroxydieldrin glucuronide and pentachloroketone (PCK). In urine of mice, the latter compound appeared only as a trace unless mice were pretreated with dieldrin. Liver and fat residues were higher in mice than in rats. In rats, however, kidney residues were much higher than in mice. This reflected the presence of PCK. Tissue residues in mice and rats were highest for dieldrin and ranged up to 3.3 ppm in liver and 66.0 ppm in fat. Maximum residues of other metabolites were: 0.51 ppm 12-hydroxydieldrin; 6.11 ppm PCK; <0.18 ppm photodieldrin; and 0.020 ppm trans-dihydroaldrindiol (Hutson, 1976).

In studies with protein derived from rat blood, binding of dieldrin was shown to be of a nonspecific hydrophobic nature (Skalsky and Guthrie, 1977).

A single dose of ^{14}C-labeled dieldrin was given by stomach tube to Sprague-Dawley rats. The dose was quickly absorbed and transported to the liver. Only a portion was metabolized and excreted. The major portion was redistributed and stored in adipose tissue (Iatropoulos et al., 1975).

After ^{14}C-aldrin was intramuscularly injected into Atlantic salmon fry (Salmo salar), 45% of the aldrin was gone after one day and less than 10% of the aldrin remained after 8 weeks. About 50% of the aldrin residues were oxidized to dieldrin within 2 days and 90% in 14 days (Addison et al., 1976).

In channel catfish (Ictalurus punctatus) exposed continuously to dieldrin, equilibrium between uptake and elimination was reached in 56 days at 13 and 27 ppt but not until after 70 days when the exposure level was 49 ppt (Shannon, 1977).

In the earthworm (*Lumbricus terrestris* L.), aldrin epoxidation occurred primarily in the intestine; and electron microscopy was used to identify the microsomal fraction as the locus of aldrin epoxidase. The involvement of cytochrome P-450 was suggested by CO inhibition of the epoxidase (Nelson et al., 1976b).

With midge (*Chironomus riparius*) larvae, piperonyl butoxide inhibited mixed function oxidase *in vivo* and *in vitro*, thereby preventing dieldrin formation (Estenik, 1978). Aldrin epoxidation was observed in six species of saturniid larvae. The epoxidase activity was higher in the midgut microsomal fractions from ultimate-stage larvae (Krieger et al., 1976c). In *Prodenia litura* (Lep., Noctuidae), aldrin was converted to the epoxide dieldrin by a mixed-function oxidase that requires O_2 and NADPH (Riviere and Fernandez, 1978).

Crops were cultivated in outdoor boxes in soil treated with ^{14}C-labeled aldrin. In the second year, crops were rotated and, additionally, wheat was grown in soils retreated with aldrin. The main product in soil and plants was identified as dieldrin. Much of the radioactivity in plants and soil resided in a mixture of hydrophilic material. The main component was identified as dihydrochlordene dicarboxylic acid. *Trans*-aldrindiol was identified in the leaching water but not in soil or plants. Another unidentified compound appeared in the upper soil layers and in plants, particularly sugar beets. Highest photodieldrin levels were found in leaves or straw of plants and ranged from 5 to 10% of the total residues. Photoaldrin was not detected in plants and only in low amounts in soils. In the soils there were radioactive products unextractable with organic solvents. About 55% of these residues became soluble when the soil was treated with dilute ammonia or sodium hydroxide. This was identified as dihydrochlordene dicarboxylic acid (Scheunert et al., 1977).

In soil treated with aldrin, residues of dihydrochlordene increased with depth whereas residues of aldrin and dieldrin were negligible below 15 cm (Stewart and Gaul, 1977). A survey of soil bacteria has shown that many are capable of epoxidation of aldrin to dieldrin. Twenty-two strains comprised of the following microorganisms converted aldrin to exo-dieldrin (Ferguson and Korte, 1977).

Bacillus sp. 1042
Bacillus cereus UFW-2
Bacillus subtilis 4
Thermoactinomyces sp. 1033
Micromonosporo sp. 1040
Nocardia sp. UFM-48
Nocardia sp. UFM-30
Pseudomonas fluorescens 1441
Pseudomonas fluorescens 1175
Pseudomonas fragi 1127
Mycobacterium phlei
Streptomyces sp. 1038
SB-4 (Motile, rod-shaped, gram-negative bacteria)
OOM-3 (Motile, rod-shaped, gram-negative bacteria)
OOW-2 (Motile, rod-shaped, gram-negative bacteria)
MIM-13 (Motile, rod-shaped, gram-negative bacteria)

Pseudomonas putida 1065	MNAP-2 (Motile, rod-shaped, gram-negative bacteria) P-5 (Motile, rod-shaped, gram-negative bacteria) P-7 (Motile, rod-shaped, gram-negative bacteria) P-9 (Motile, rod-shaped, gram-negative bacteria) P-10 (Motile, rod-shaped, gram-negative bacteria)

When aldrin is applied to soil, after one year about two-thirds of the residue is present as dieldrin. This rises to 90% after three years. The pattern of loss observed in these studies indicated that the accumulated residue, after repeated annual application, would approach a finite value which would not be exceeded. The following equation was derived:

$$R_a = \frac{fd\,[1-(1-p)^n]}{p}$$

where $f = 0.25$ and $p = 0.44$. This gives .57d or 57% of the level occurring immediately after the first application (Elgar, 1974).

Aldrin and dieldrin were exposed to UV light in a laboratory reactor. Aldrin underwent epoxidation to dieldrin and to photoaldrin. Photoaldrin was epoxidized to photodieldrin. Photodieldrin, which formed from dieldrin as well as photoaldrin, did not undergo further reaction and apparently represents an end-product of aldrin photodecomposition (Moilanen and Crosby, 1974).

Photodieldrin was administered in feed or by injection to male rabbits. Urine and feces were collected for every 24 h for 9 d. About 10-13% of the administered dose was released by β-glucuronidase from the aqueous phase of the urine analysis; about 2 to 3%, by 1N HCl. In addition to photodieldrin, six metabolites were observed with TLC. Of these, photodieldrin *trans*-diol and photodieldrin ketone were identified by means of IR and GC-MS (Reddy and Khan, 1978).

Dieldrin volatilization from soil was investigated in sandy loam and sand. After 60 days at 25C, only 8.9% of the dieldrin had been lost by volatilization from sandy loam soil while 34.2% was lost from sand (Caro et al., 1976). In other soil studies, dieldrin volatilized rapidly during the first 12 h after application; and after 30 days, only 11% of applied dieldrin remained (Taylor et al., 1977). The disappearance rate of dieldrin from soil followed the equation

$$D = 2.72 - 0.20\ (\pm 0.09)T.$$

This equation indicates 95% disappearance in 13 years (Freeman et al., 1975). Under the elevated temperature conditions of a cotton field in Sudan, dieldrin disappearance was more rapid. Seven weeks after application to a cotton field, less than 8% of applied dieldrin was present (El Zorgani, 1976). Other studies have also shown that under subtropical conditions, dieldrin persistence in soil is shortened with a calculated 50% disappearance in 7.5 months (Talekar et al., 1977b).

Within one day after dieldrin application to an orchard-grass pasture, residues of photodieldrin were found. After rising to a maximum of 51 ppm after 5 days, these residues declined to 9 ppm after 107 days. While photodieldrin exhibited only about 1% of the volatility of dieldrin, over the first three weeks, about 26 g/ha of photodieldrin volatilized (Turner et al., 1977).

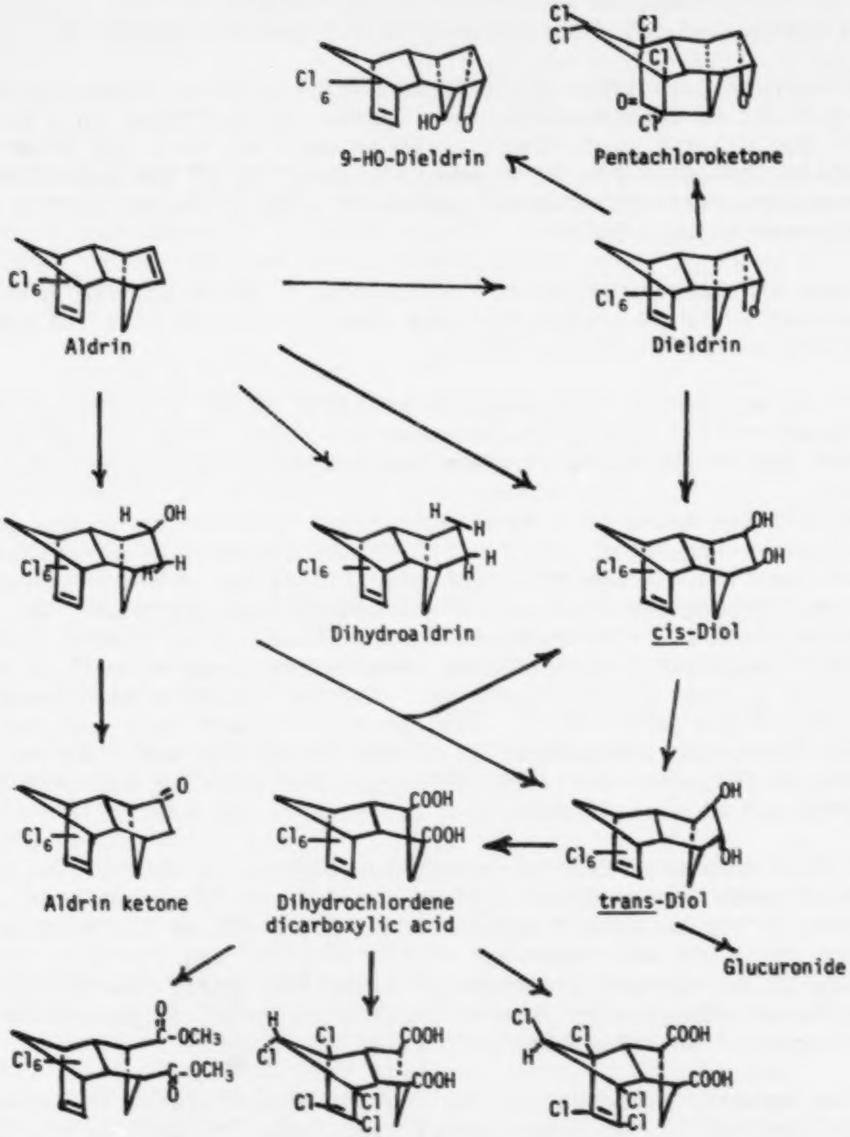
When incubated with ovine rumen fluid, 5.2% of the dieldrin added was converted to an olefin that was identified by GLC-MS and chemical reactions as aldrin (Ivie, 1976).

At points remote from areas of dieldrin usage, analyses of air samples taken in 1973 showed the presence of dieldrin and the absence of aldrin and the photoisomers of these two compounds (Baldwin et al., 1977).

Aldrin was added to a model ecosystem. Conversion to the epoxide dieldrin was rapid. Of the ^{14}C stored in the various organisms, 95.9% of the total in the fish Gambusia affinis was dieldrin; 91.6%, in the snail Physa; and 85.7%, in algae Oedogonium cardiacum. Two metabolites identified as 9-hydroxydieldrin and 9-ketodieldrin were found in algae, snail and fish. Dieldrin was observed in these as well as the mosquito Culex pipiens quinquefasciatus. Another compound was thought to be the trans-dihydroaldrindiol. Similar results were obtained when dieldrin was used. The magnification of aldrin in fish was 3140 and in snail was 44,600. For dieldrin, this was 5957 for fish and 11,149 for snail (Metcalf et al., 1973b).

Into a model terrestrial ecosystem, aldrin was added. Two weeks after corn seeds were planted, aldrin residue was 27% greater in the plant than in the soil at planting time. About 78% of the residue was in the roots and was comprised of aldrin (33%) and dieldrin (49%). On day 15, a vole was introduced. After five days, the residue in the vole was 70% greater than initial soil concentration and consisted of 2% aldrin and 89% dieldrin (Cole et al., 1976).

The capacity of soil fungi to degrade photodieldrin was studied in culture media. Of nine species used, only Trichoderma viride appreciably degraded photodieldrin. Within 4 to 5 weeks, 32-41% of the applied radiolabel was metabolized to water-soluble compounds. When aldrin, dieldrin or chlordane were added to the culture media, the amount of water-soluble compounds decreased, indicating decreased degradation (Tabet and Lichtenstein, 1976).


9-HO-Dieldrin
Pentachloroketone
Aldrin
Dieldrin
Dihydroaldrin
cis-Diol
Aldrin ketone
Dihydrochlordene dicarboxylic acid
trans-Diol
Glucuronide
Cl6
HO
OH
H
COOH
O
C-OCH3
Cl

In houseflies, metabolism of photodieldrin was higher in females than in males. Three metabolites were observed. Two were identified as *trans*-photoaldrindiol and photodieldrin ketone (Reddy and Khan, 1977a). In the American cockroach, the major metabolite of photodieldrin was 2-ketodieldrin (Kadous, 1978).

For 21 days, endrin was fed in the diet to two lactating cows. Endrin intake was equivalent to 0.1 mg/kg total diet. Between the 4th and 9th day, equilibrium was reached between intake and excretion via milk, urine and feces. Milk, fat and muscle residues consisted primarily of unchanged endrin and peaked at 0.003-0.006, 0.1 and 0.001-0.002 mg/kg, respectively. Analysis of collected urine indicated the absence of endrin. The major metabolite found was *anti*-12-hydroxyendrin. Small amounts of the *syn*-isomer, 12-ketoendrin, 3-hydroxyendrin and the *anti*-12-hydroxyendrin glucuronide were also observed. In feces in addition to endrin, 12-ketoendrin and *anti*-12-hydroxyendrin were found (Baldwin et al., 1976).

After oral administration of endrin to rabbits, analyses showed that 50% of the administered compound was excreted unchanged in the feces. Urine contained a mixture of polar metabolites identified as: *anti*-12-hydroxyendrin, *syn*-12-hydroxyendrin, and 4,5-*trans*-isodrin-4,5-dihydrodiol and their glucuronides and sulfates; 3-hydroxyendrin; and 12-ketoendrin (Bedford et al., 1975b).

Endrin was orally administered to susceptible (S) and resistant (R) strains of pine mice. Although there were quantitative differences in the amounts of urinary metabolites, the most striking difference was the absence of one metabolite from R strain autoradiograms (Petrella et al., 1975). Chemical ionization mass spectrometry and infra-red spectroscopy were used to identify *anti*-12-hydroxyendrin from feces and urine and as a product of *in vitro* hepatic microsomal metabolism. Two other metabolites have been tentatively identified as 3-hydroxyendrin and a cyclic hemiketal, 4(5)-hydroxyendrin (Petrella et al., 1977).

Studies with mosquito fish (*Gambusia affinis*) showed that endrin uptake was greater in susceptible than in resistant fish. At high lethal concentrations, endrin also entered the brain at a lower rate in resistant fish and accumulated in the liver (Fabacher and Chambers, 1976; Scales and Yarbrough, 1975). The biologic half-life of endrin in channel catfish has been calculated variously as 6 and 12 days. Size and feeding rate could account for the difference (Jackson, 1976).

Endrin was administered in corn oil to laying hens for 21 weeks at a rate of about 0.13 mg/kg total diet. Ingestion and excretion reached a near-balance between 16 and 20 weeks. Residues in eggs were composed of unchanged endrin in the yolk and peaked at 0.11 to 0.18 mg/kg. Residues in other tissues, except kidney and liver, were also primarily unchanged endrin. The major metabolite observed in excreta was *anti*-12-hydroxyendrin. A small amount of the sulfate conjugate was also found. No other metabolites were identified (Baldwin et al., 1976).

When endrin was administered to the American cockroach, the most toxic metabolite was identified as 2-hydroxyendrin (Kadous, 1978).

In soils, endrin degradation was greater under flooded conditions than under non-flooded conditions. Using ^{14}C-endrin and autoradiography, six degradation products were observed in flooded soils and four in non-flooded soil. Only ketoendrin was identified (Gowda and Sethunathan, 1976 and 1977).

Photoisodrin was rapidly metabolized by mice. In four days, about 10% of the administered dose was excreted in urine. Four unidentified metabolites were present in urine, three probably as glucuronide or sulfate conjugates. Feces, however, was the major route of excretion of photoisodrin. Five metabolites were present in the organic extracts. Acid hydrolysis of the aqueous phase released four metabolites. None were identified. Houseflies also metabolized photoisodrin to compounds both free and conjugated. None were identified (Reddy and Khan, 1976 and 1977b).

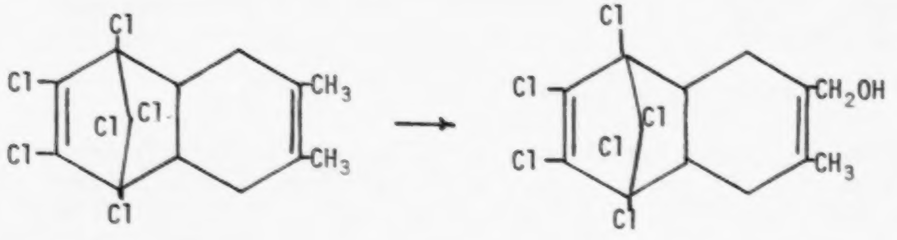
Dihydroisodrin was metabolized *in vivo* by black cutworm (*Agrotis ypsilon*) and cabbage looper (*Trichoplusia ni*) larvae and *in vitro* by homogenates of larvae. Removal of gut contents prior to homogenation appreciably increased the hydroxylation activity. The only metaboilite observed was 6-*exo*-hydroxydihydroisodrin. The hydroxylase system seemed to be concentrated in the microsomal fractions of cell-free tissue homogenates and exhibited a requirement for oxygen and NADPH for maximum enzyme activity (Thongsinthusak, 1975; Thongsinthusak and Krieger, 1976).

Hydroxylation of endrin was observed in six species of saturniid larvae. This activity was highest in midgut microsomal fractions from ultimate-stage larvae (Krieger et al., 1976c).

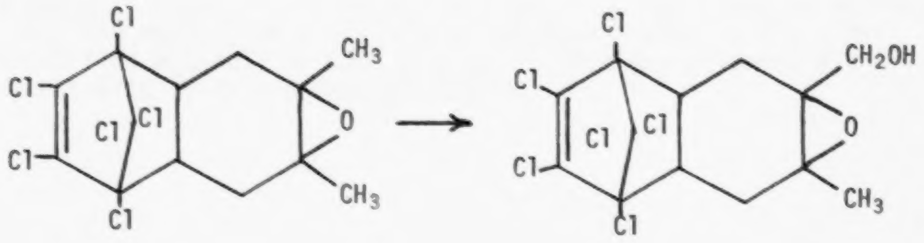
In a model ecosystem, endrin bioaccumulation was highest in the snail (*Physa* sp.). Four metabolites were observed but not identified. One was believed to be 9-hydroxyendrin (Metcalf et al., 1973b).

Aldrin-Dieldrin Analogs

The metabolism of analogs of aldrin (DMO) and dieldrin (DME) were studied with liver supernates + NADPH obtained from Wistar and CD strains of rats. DMO was not metabolized to the corresponding epoxide. The mass spectrum of the metabolite was consistent with a hydroxymethyl derivative of DMO. When DME was used with preparations from female rats, the main metabolite was a ring hydroxylated epoxide. With male rat supernate, small quantities of the same compound formed but the major metabolite had a mass spectrum indicative of a hydroxymethyl epoxide. No hydrolysis of the oxirane ring was detected (Hassall et al., 1978).



DMO



DME

AMCHEM Z-2088 [Dimethyl heptyl 1-hydroxy-p-menth-2-yl ammonium bromide]

When this compound was applied to grapefruit trees at a level of 30 g per tree, the half-life in the leaves was 10.8 days (Newhall and Buslig, 1977).

AMIBEN (Chloramben) [3-Amino-2,5-dichlorobenzoic acid]

Giant foxtail (Setaria faberii Herrm.) was treated with amiben. During clean-up of the methanol extracts on Florisil columns, transesterification occurred producing a methyl ester of amiben. The ester metabolite was isolated and identified as 1-O-(3-amino-2,5-dichlorobenzoyl)-β-D-glucose (Frear and Swanson, 1977). Subsequent studies have indicated that this glucoside is actually of the α configuration (Frear et al., 1978).

Tissue sections from resistant and susceptible plants were used to assess their ability to form glucose metabolites. The N-glucoside as well as the O-glucoside were formed by root and hypocotyl or shoot tissues from the following plants:

Resistant	Intermediate	Susceptible
morningglory	corn	velvet leaf
squash	cucumber	barley
snapbean		giant foxtail
soybean		barnyard grass

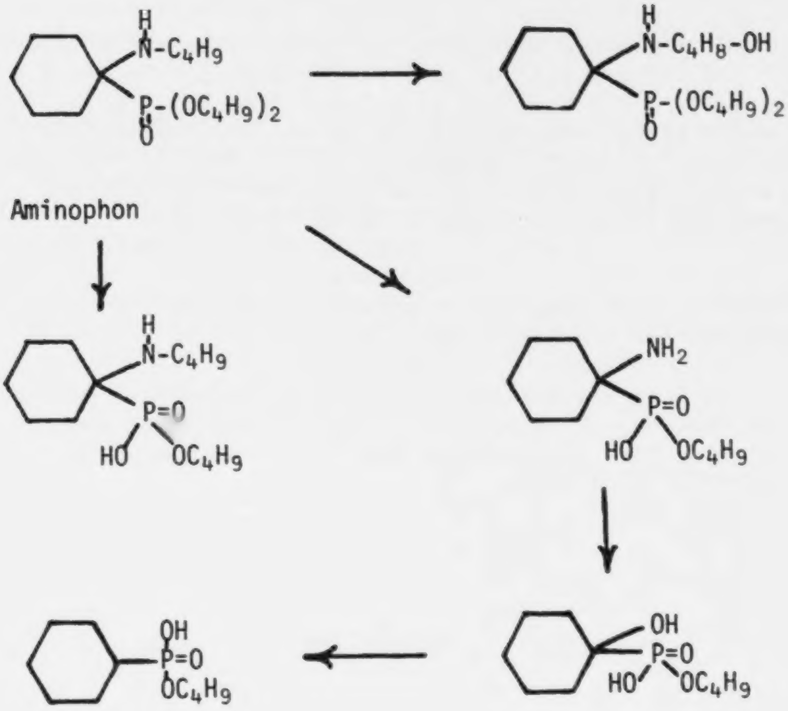
(Frear et al., 1978).

Earthworms (Lumbricus terrestris) were collected from plots which had been treated with a single herbicide over a period of years as well as from control plots. These were placed in a glass container with sand after injection of ^{14}C-amiben. In addition to unchanged amiben and some unextractable ^{14}C, five metabolites were observed with control worms and nine with treated area worms. In each case one metabolite was identified as 2,5-dichloroaniline (Chio and Sanborn, 1978).

On soil amiben phytotoxicity to oats was decreased by photodecomposition. Two unidentified compounds were observed. Some decarboxylation did occur (Fickle, 1974). 2,5-Dichloroaniline was found in extracts of sand and worms from plots treated with chloramben. Six other unidentified metabolites were present in worm extracts and eight in sand extracts (Chio and Sanborn, 1978).

AMINOPHON (Trakephon) [*O*,*O*-Di-*n*-butyl-(1-*n*-butylaminocyclohexyl) phosphonate]

^{32}P-Aminophon was administered in oil to lactating cows. The $t_{1/2}$ in blood, milk and urine was 17-20 h. Binding of aminophon and/or its metabolites to blood proteins was observed. *In vitro*, the $t_{1/2}$ of aminophon was 95 minutes. In milk, 20-25% of the ^{32}P was extractable. Binding with milk proteins was noted. In urine the metabolite concentrations were higher than in blood and milk by a factor of 10^2. About 20-25% of the metabolites in urine were extractable in one pass. After acidification with HCl about 50% of the activity was extractable. Urinary metabolites identified included: desbutyl aminophon (I), the *n*-1-hydroxybutyl aminophon, and *O*-*n*-butyl 1-aminocyclohexylphosphonate. Two other compounds observed, but not identified, are believed to be *O*-*n*-butyl 1-hydroxycyclohexylphosphonate and *O*-*n*-butyl cyclohexylphosphonate (Dedek et al., 1978a).

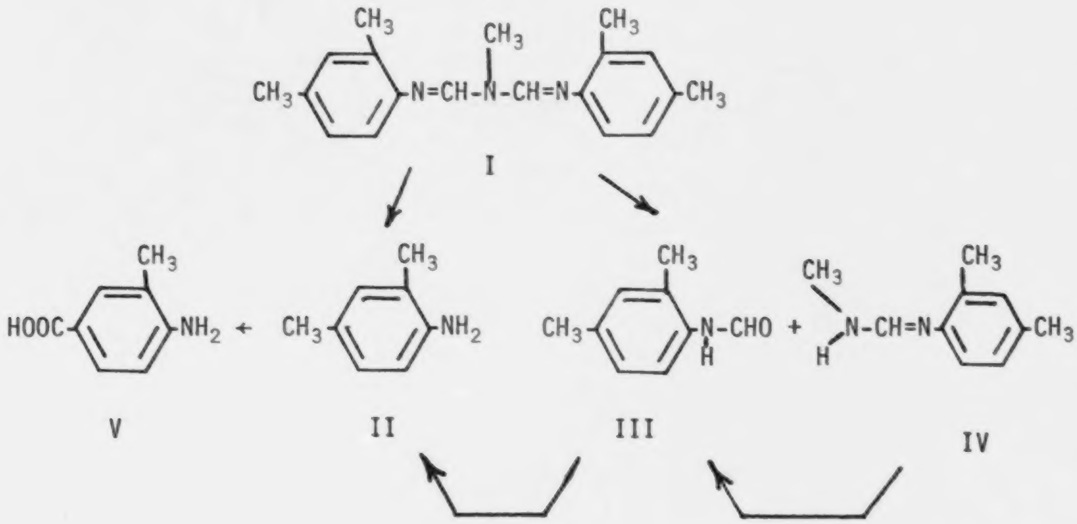

H
N-C4H9
P-(OC4H9)2
O
H
N-C4H8-OH
P-(OC4H9)2
O
Aminophon
H
N-C4H9
P=O
HO
OC4H9
NH2
P=O
HO
OC4H9
OH
P=O
OC4H9
OH
P=O
HO
OC4H9

AMITRAZ [1,5-Di-(2,4-dimethylphenyl)-3-methyl-1,3,5-triazapenta-1,4-diene]

Bacteria capable of degrading amitraz were obtained from cattle dipping tanks and were identified as *Pseudomonas* sp. and *Achromobacter* sp. The bacteria, however, were not able to use amitraz as a substrate or as an energy source. No metabolites were identified. Degradation did not occur at pH >11.5 (Baker and Woods, 1977).

Amitraz was incubated with mixed cultures of bacteria from cattle dip tanks. The primary path of amitraz degradation yielded 2,4-dimethylaniline (II). This compound also arose from 2,4-dimethylformanilide (III) which arises when amitraz is split into the anilide plus *N*-2,4-dimethylphenyl *N*'-methylformamidine (IV). This latter compound was also further degraded to 2,4-dimethylformanilide (Allcock et al., 1978). In plants the first step appears to be formation of compound IV which then yields III. In animals, 4-amino-3-methylbenzoic appears in the urine, arising from III, probably via compound II. This latter has not, however, been observed in plants or animals (P. Oxley, private communication in Allcock et al., 1978).

When ^{14}C-amitraz was applied to *Boophilus microplus*, penetration occurred readily. Cleavage to III and IV and large amounts of polar material occurred. Compound II and CO_2 were also produced (Schuntner and Thompson, 1978).



AMITROLE (ATA) [3-Amino-1,2,4-triazole]

A single dose of 50 mg/kg of 5-^{14}C-labeled amitrole was administered orally to rats. Urine and feces were collected. Unchanged amitrole was the main compound found in urine in the initial 24 h. Subsequently two metabolites were isolated from urine. Comparison with synthetic compounds, using thin-layer and paper chromatography and IR and mass spectroscopy, identified these compounds as 3-amino-5-mercapto-1,2,4-triazole and 3-amino-1,2,4-triazole-5-mercapturic acid (Grunow et al., 1975).

In other studies with rats, unaltered amitrole and three metabolites were found in the urine of the rats. One was identified as the alanine conjugate. Another compound present in rat urine has also been found in bean plants. A third compound observed was found in beans and *E. coli* (Franco and Muncio, 1975).

Pure cultures of amitrole-degrading bacteria were isolated from soil. Nine isolates were Gram-positive rods (*Bacillus* spp. and *Corynebacterium* spp.) and one was a *Pseudomonas* sp. (Campacci et al., 1977).

ANILINE

Rats metabolized 4-nitroaniline primarily to 4-phenylenediamine (about 26%) and 2-amino-5-nitrophenol (43%) but no 4-aminophenol was detected (Mate et al., 1967).

When tomato, barley or wheat plants were exposed to 4-chloroaniline (4-CA) and 3,4-DCA, about 90-95% of these materials were found in the roots. In carrots, the distribution was about the same in roots and in upper parts of the plants (Fuchsbichler et al., 1978a).

Algae were grown in nutrient solution to which *p*-chloroaniline had been added. Analyses showed the presence of *p,p*'-dichloroazobenzene and *p,p*'-dichloroazoxybenzene in the algae; *p*-chloroformanilide and *p*-chloroacetanilide in the nutrient medium; and three unidentified products (2 in the medium and one in the algae) (Anagnostopoulos et al., 1978).

^{14}C-3,4-DCA was applied to soil and barley was planted immediately thereafter. Potatoes were grown in the soil in the following year. Recovery of ^{14}C from soil, plants and leaching water after one year (69.8%) was comparable to the second year (67.1%). The products from soil identified by chromatographic retention data and MS were: 3,3',4-trichloroazobenzene; 3,4-dichloroformanilide; 3,4-dichloroacetanilide; and 6-hydroxy-3,4-dichloroacetanilide. In plants only the azobenzene and the hydroxyanilide were observed (Viswanathan et al., 1978b).

When rice plants were treated hydroponically with ^{14}C-3-chloroaniline or ^{14}C-DCA, evidence indicated that lignin fractions contained more than half of the ^{14}C. When model synthetic lignin-chloroaniline polymers and bound residue fractions from rice plant roots were subjected to pyrolysis, recovery of ^{14}C-chloroanilines was greater than 70% (Balba et al., 1977; Still et al., 1978).

With a laccase isolated from the soil fungi *Rhizoctonia praticola*, incubation with 2,4-DCA and 2,4-dichlorophenol produce a trimer consisting of two phenols and one aniline molecule (Bollag et al., 1978a).

Rice root callus suspension culture in Yatazawa growth medium took up 3,4-DCA rapidly. When ^{14}C-ring-labeled DCA was used, labeled compounds were released into the medium. Four peaks, not identified, were observed in the methanol extractable portion of the tissue. Base hydrolysis released DCA. MS indicated masses in excess of 500 and IR, UV, and chromogenic spray reagents plus TLC indicated compounds with a quinone structure (Abe, 1975). Nitric acid digestion of a bound residue from rice (*Oryza sativa* L.) root, hydroponically treated with 3,4-DCA, yielded three volatile compounds identified as 1,2-dichlorobenzene, 1,2-dichloro-3-nitrobenzene, and 1,2-dichloro-4-nitrobenzene. Nitric acid digestion of 3,4-DCA, its acetanilide or N-glucosamine did not give these products. However, 1,2-dichlorobenzene and 1,2-dichloro-4-nitrobenzene were obtained with nitric acid digestion of N-ethyl 3,4-DCA (Norris and Still, 1974).

In other studies, *Ps. aurantiaca* strains metabolized 3,4-dichloroaniline at varying rates to TCAB (Surovtzeva and Funtikova, 1978). In an anaerobic medium, Paracoccus sp. caused formation of 1,3-bis(p-chlorophenyl)triazene (Minard et al., 1977).

The soil fungus *Fusarium oxysporum* Schlecht metabolized chloropropham and 2-, 3-, and 4-chloroaniline in isolated cultures. The culture solutions contained o-hydroxylated chloroanilines and chlorinated benzoxazolinones. A metabolite of 4-chloroaniline was identified as 2-amino-5-chlorophenol. Chloroaminophenols were also detected as metabolites of 2- and 3-chloroaniline and from chloropropham (Fletcher and Kaufman, 1975).

When 4-chloroaniline was incubated with nonsterile soil or autoclaved soil inoculated with the fungus *Fusarium oxysporum* Schlecht, identified degradation products extracted included: 4,4'-dichloroazobenzene; 4,4-dichloroazoxybenzene; 4-chloronitrobenzene; 4'-chloroacetanilide; and 4-nitrocatechol diacetate. Several unidentified compounds were also present (Kaufman and Fletcher, 1974a). Degradation of 4-nitrocatechol in soil proceeded rapidly with $^{14}CO_2$ being evolved within 7 days (Kaufman and Fletcher, 1974b). In other studies, incubation of 4-chloroaniline with soil microorganisms produced a pigment identified as 7-chloro-2-amino-3H-phenoxazin-3-one (Briggs and Walker, 1973).

DCA-humus complexes in soil shifted gradually with time to a nonhydrolyzable form. Studies with *A. versicolor* showed that these nonhydrolyzable DCA residues were oxidized at rates comparable to those with hydrolyzable or absorbed DCA (Hsu and Bartha, 1976).

Mineralization of 2-chloro-, 3-chloro-, 4-chloro- anilines and 3,4-DCA in soil was studied. Over a 16-week period, 3-chloroaniline exhibited the highest rate while 3,4-DCA was lowest. After the study, only a small amount of ^{14}C was extractable from the soil; but, after basic hydrolysis, a large amount of the soil-bound radioactivity was identified as unchanged chloroanilines (Fuchsbichler et al., 1978b; Suss et al., 1978).

When 4-chloroaniline was incubated with H_2O_2 and chloroperoxidase, 4-chloronitrosobenzene formed rapidly. The pH optimum was 4.4 with a $K_m = 8.1 \times 10^{-4}$ M. 4-Chlorophenylhydroxylamine conversion to the nitroso compound by this enzyme was even more rapid (Corbett et al., 1978).

UV irradiation of 3,4-DCA produced 2-chloro-5-aminophenol in high yield (78%). In water, about 3% of DCA decomposed to 3-chloroaniline (Miller et al., 1978).

ANTIMYCIN

Liver homogenates of yellow perch, white bass, bluegill, rainbow trout, black bullheads, carp, rat and pig inactivated antimycin at rates that differed by as much as tenfold. One type of degradation product, isovalerylantimycin A_3, occurred from hydrolysis of the fatty acid side chain from the lactone ring. The other type resulted from hydrolysis of the ester bond of the lactone ring that involved the threonine hydroxyl group. Other products not characterized were observed by GC (Hinz, 1973).

ANTOR (H-22234) [Ethyl *N*-(2-chloroacetyl) *N*-(2,6-diethylphenyl)glycine]

DUAL (Metolachlor) [2-Chloro-*N*-(2-ethyl-6-methylphenyl)-*N*-(2-methoxy-1-methyl ethyl)acetamide]

The metabolism of antor by resting cells of the fungus *Chaetomium globosum* was studied. GLC-MS was used to identify metabolites which included the following:

II. ethyl 2,6-diethylphenyliminoacetate

III. 2-chloro-*N*-(2,6-diethylphenyl)acetamide

IV. *N*-chloroacetyl-2,3-dihydro-7-ethylindole

V. ethyl *N*-chloroacetyl-*N*-(2-ethyl-6-vinylphenyl)glycine

VI. *N*-chloroacetyl-*N*-(2-ethyl-6-vinylphenyl)glycine

VII. ethyl 7-ethylindolinylacetate

VIII. ethyl *N*-(2-hydroxyacetyl)-*N*-(2-ethyl-6-vinylphenyl)glycine

The identification of compounds II and VII was not complete. The possibility that either of these compounds could be ethyl *N*-(2-ethyl-6-vinylphenyl)glycine was not eliminated (McGahen and Tiedje, 1978).

Studies with the antor analog metolachlor (dual) were also conducted with the fungus *Chaetomium globosum*. Compounds produced by this organism when incubated with metolachlor are summarized below:

II. 2-chloro-*N*-(2-ethyl-6-methylphenyl)-*N*-(2-hydroxy-1-methylethyl) acetamide

III. 2-chloro-*N*-(2-ethyl-6-methylphenyl)acetamide

IV. *N*-(2-methoxy-1-methylethyl)-2-methyl-6-vinylaniline

V. *N*-(2-methoxy-1-methylethyl)-2,3-dihydro-7-methylindole

VI. 8-ethyl-3-hydroxy-*N*-(2-methoxy-1-methylethyl)-2-oxo-1,2,3,4-tetrahydroquinoline

VII. 8-ethyl-3-hydroxy-*N*-isopropyl-2-oxo-1,2,3,4-tetrahydroquinoline

VIII. 2-hydroxy-*N*-(2-methoxy-1-methylethyl)-*N*-(2-methyl-6-vinylphenyl) acetamide

IX. N-(2-methoxy-1-methylethyl)-8-methyl-2-oxo-1,2,3,4-tetrahydroquinoline

(McGahen and Tiedje, 1978).

ANTU [α-Naphthylthiourea]

After administration to rats, ^{14}C-antu distribution and excretion was observed. Radioactivity increased in liver and kidney for 8 h and then decreased. About 80% of the activity present in serum and pleural fluids was contained in the albumin fraction. Within 20 h, over 40% of the administered activity appeared in urine. Feces contained less than 1%. Three metabolites were observed but not identified (Patil and Radhakrishnamurty, 1977).

Studies indicated that ANTU underwent metabolism and activation *in vitro* by lung and liver microsomes to an intermediate that bound to microsomal macromolecules (Boyd and Neal, 1976).

4-AP [4-Aminopyridine]

When 4-AP was incubated with pure cultures of *Pseudomonas fluorescens*, *Enterobacter aerogenes*, *Aspergillus niger*, *Streptomyces griseus*, or *Agrobacterium tumefaciens*, no significant degradation of the compound occurred. When incubated in three different soils, between 6 and 24% of the applied 4-AP-^{14}C was recovered after 60 days as $^{14}CO_2$. In 2 flooded soils, 21-24% of the radioactivity was lost after 60 days. On moist soil, 16% of the radioactivity was recovered as $^{14}CO_2$ after 70 days when chopped corn containing 3% 4-AP-2-^{14}C was added (Betts et al., 1976).

ARSENICALS

Urine of copper smelter workers, exposed to inorganic arsenic mainly in the form of arsenic trioxide, was analyzed. All workers excreted arsenic primarily as methylated arsenicals, 50% as dimethylarsinic acid and 20% as methylarsonic acid (Smith et al., 1977).

After human ingestion of arsenite rich wine, 10% of the arsenic was excreted as methylarsonic acid and dimethylarsinic acid. Ingestion of arsenate-rich water produced elevated levels of arsenate and dimethylarsinic acid. However, when crab meat containing organoarsenic was ingested, none of these compounds was observed at elevated levels until after digestion of the urine with hot 2N NaOH. Then high levels of dimethylarsinic acid were observed (Crecelius, 1977).

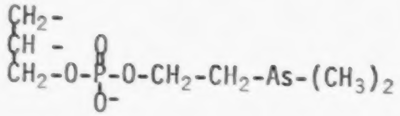
The metabolism of inorganic arsenic was studied in cows and dogs. When sodium arsenate was fed to cows, analyses of urine indicated the presence of methylated arsenic (MA) (maximum of 3.53 ppm) and inorganic arsenic (IA) (maximum of 1.33 ppm); feeding of potassium arsenite produced maxima of 4.78 ppm MA and 1.57 ppm IA. In urine of dogs, the MA peaked at 6.23 ppm and IA at 10.48 ppm after arsenate feeding; 5.03 ppm MA and 5.16 ppm IA after arsenite feeding (Lakso and Peoples, 1975).

Mice were administered i.m. 1.3 mg As(III)/kg after exposure to a toxic concentration of sodium arsenite [250 mg As(III)/l] for 2, 6 and 8 days. Whereas mice not exposed to the treated drinking water excreted one-half the i.m. administered As(III), those mice previously exposed to the treated water excreted 80% of the applied As(III) as As(V) in 2 days; more than 95%, after 4 days; and after 8 days only traces of As(III) were present (Bencko et al., 1976).

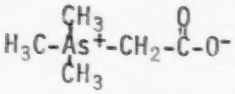
When inorganic arsenic was fed to brown trout (*Salmo trutta*), the arsenic was converted to an organic form. The data are consistent with the hypothesis that this conversion is mediated by the intestinal flora (Lunde, 1973; Penrose, 1975). Sea urchins (*Strongylocentrotus droebachiensis*) converted inorganic As to an organic form. Spectroscopic analyses indicated a tetramethylarsonium ion but this could not be confirmed (Penrose et al., 1977).

Studies were undertaken to characterize arsenicals formed by *Daphnia magna* and *Tetraselmis chuii* from inorganic arsenate. *T. chuii* efficiently incorporated arsenic and formed a lipid-soluble arsenical. *Daphnia magna* formed an arsenical that migrated with phosphatidylethanolamine and exhibited properties consistent with the presence of arsenocholine in the lipid (I or II) (Irgolic et al., 1977).

Studies with various marine materials indicated that the organoarsenicals present are of a similar chemical nature: soluble in ethanol, generally quite stable to boiling 6.6 N HCl, and give a blue ninhydrin reaction. Work with a material from cod liver also demonstrated strong UV absorption at about 260nm and an IR spectrum with aromatic characteristics and hydroxyl and amino functions (Lunde, 1975a and b). Analyses of lobsters, mussels and stingrays taken from waters of W. Australia indicated the presence of arsenic in the tissues. After extraction of the tissues and digestion and distillation of volatile arsenicals, the arsines were identified as arsine (5%), dimethylarsine (60%), and trimethylarsine (35%) (Edmonds and Francesconi, 1977a). In other studies, the arsenical obtained from the Australian western rock lobster (*Panulirus longipes cygnus* George) has been identified from single crystal X-ray structure determination and comparison with a synthetic specimen as arsenobetaine (III).

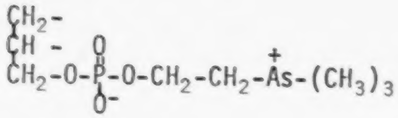
I


$$\begin{array}{l} \mathrm{CH_2{-}} \\ \mathrm{CH{-}} \\ \mathrm{CH_2{-}O{-}\underset{O^-}{\overset{O}{P}}{-}O{-}CH_2{-}CH_2{-}As{-}(CH_3)_2} \end{array}$$



$$\mathrm{H_3C{-}\underset{CH_3}{\overset{CH_3}{As^+}}{-}CH_2{-}\overset{O}{C}{-}O^-}$$

Arsenobetaine (III)

II


$$\begin{array}{l} \mathrm{CH_2{-}} \\ \mathrm{CH{-}} \\ \mathrm{CH_2{-}O{-}\underset{O^-}{\overset{O}{P}}{-}O{-}CH_2{-}CH_2{-}\overset{+}{As}{-}(CH_3)_3} \end{array}$$

The natural and synthetic samples had the same R_f value; m.p. was not depressed; and mass spectra were identical (Edmonds et al., 1977).

The production of a volatile arsenical from moldy wall-paper has been observed for more than 100 years (Basedow, 1846). Studies to identify this gas were conducted by Biginelli, 1901; Emmerling, 1896; Klason, 1914; Wigren, 1924. Bibliographics on arsenic molds have been prepared by Maasen, 1902. In addition to *P. brevicaule*, identified microorganisms that produce a volatile arsenic gas include *Aspergillus glaucus*, *A. virens*, *Mucor mucedo*, and *M. ramosus* (Gosio, 1892, 1897 and 1901). The production of arsine from arsenic salts by saprophytic fungi was reported (Gosio, 1892, and 1897; Sanger, 1894; Biginelli, 1900a and b; Maasen, 1902). The dermatophyte *Trichophyton rubrum* also produced a garlic-like odor when incubated with arsenate and arsenite. This was identified as arsine (Zussman et al., 1961). Other studies had showed that all isolates of the fungi *Lenzites trabea* and *L. saepiaria* produced a garlic-like smell, presumably trimethylarsine when incubated with arsenic trioxide (Merrill and French, 1964). Several *Aspergillus* spp., *Penicillium* spp., and *Scopulariopsis* spp. and a *Mucor* sp. were also capable of methylating arsenicals (Challenger, 1945). The volatile gases produced when sodium arsenate was added to soil were identified as dimethylarsine and trimethylarsine by ion exchange, gas chromatography and mass spectroscopy. No monomethylarsine was observed (Woolson, 1976 and 1977a and b).

Cell extracts and whole cells of *Methanobacterium* strain M.o.H. were found to be capable of anaerobic reduction of arsenate to arsenite. This was then methylated anaerobically to produce methylarsonic acid with methylcobalamin as the preferred methyl donor. Reductive methylation of methylarsonic acid produced dimethylarsinic acid. Reduction of the latter gave dimethylarsine. Cellular extracts required ATP and hydrogen for formation of dimethylarsine (McBride and Wolfe, 1971).

Four strains of *P. brevicaule* (*Scopulariopsis brevicaulis*) were cultivated on bread-crumbs containing arsenious oxide. All produced trimethylarsine (Challenger et al., 1933).

When arsenite was added to raw sewage, arsenite disappeared. Arsenate was detected within a week. The organisms involved were identified as strains of *Alcaligenes faecalis* (Phillips and Taylor, 1976).

The production of volatile arsenicals by microorganisms was studied. Three fungi isolated from sewage were capable of forming trimethylarsine from various arsenic compounds. These studies are summarized. A *Methanobacterium* sp. found in wastewater treatment plants also formed dimethylarsine anaerobically from arsenite (Cox, 1974; Cox and Alexander, 1973).

	Organism		
Arsenical Used	*Candida humicola* (Dazewska) Diddens & Lodder	*Gliocladium roseum* Bain	*Penicillium* sp.
DMA	pH 5, 6 & 7	pH 5, 6 & 7	pH 5, 6 & 7
MMA	pH 5 & 6	pH 5, 6 & 7	pH 5, 6 & 7
Arsenate	pH 5	NF	NF
Arsenite	pH 5, 6 & 7	NF	NF

DMA = dimethylarsinic acid (cacodylic acid)
MMA = monomethylarsonic acid
NF = Trimethyl arsine not formed at pH 5, 6 or 7.

In seawater, arsenite has been shown to oxidize at measurable but slow rates with about two-fold increase for an increase of 10C in temperature. At a pH of 7.8, salinity of 35 $^{\circ}/_{\circ\circ}$, temperature of 4C, and arsenite concentration of 0.01 micromolar, the initial arsenite oxidation rate was calculated to be 6.43x10^{-5} micromoles As(III) oxidized per liter per day (or 0.023 μ moles per liter per year (Johnson and Pilson, 1975).

Studies with the coral *Pocillopora verrucosa* indicated that it could remove arsenate from solution and convert some of it to arsenite (Pilson, 1974). The freshwater green alga *Chlorella* was also able to reduce arsenate to arsenite (Blasco et al., 1971).

Marine bacteria obtained from Narragansett Bay, not identified, reduced arsenate to arsenite (Johnson, 1972). In other studies, *Skeletonema costatum* from Narragansett Bay reduced arsenate to arsenite during growth and phosphate depletion (Johnson and Burke, 1978).

In a study of methylated forms of arsenic in the environment, analyses indicated the presence of methylated arsenic in a wide variety of samples. This is summarized.

	Methylarsonic acid	Dimethylarsinic acid
human urine	+	+
lakes and ponds	+	+
well water	+	+
Tampa Bay	+	+
seashells, bird eggshells	+	+
limestone	tr	tr

(Braman and Foreback, 1973)

Arsenate was strongly sorbed by the amorphous Fe and Al in soils and leaching was minimal except at very high rates of application (Walsh and Keeney, 1974). Under reducing conditions, lead arsenate in soil was slowly converted to manganese arsenate but reformed under highly oxidized conditions. It was also possible to observe, under experimental conditions, the formation of volatile arsenicals (Hess, 1976).

In an aquatic model ecosystem, to which ^{74}As had been added, accumulation of arsenic was greatest in algae (80.5%), followed by crayfish (15.7%), gambusia (2.4%) and daphnids (1.3%). Four unidentified arsenicals were observed (Woolson et al., 1976). Lower food chain organisms (algae and daphnia) bioaccumulated more cacodylic acid and dimethylarsine than did higher food chain organisms (snails and fish) (Isensee et al., 1973).

ARSENICALS

ARSANILIC ACID [4-Aminobenzenearsonic acid]

In soil, under flooded and nonflooded conditions, arsanilic acid disappeared rapidly. Total arsenic content remained constant. Conversion of arsanilic acid to arsenate occurred under flooded conditions as well as at 75% field capacity. Salts of arsanilic acid seemed to form with aluminum, iron and calcium as with arsenate (Woolson, 1974).

When applied to soil, arsanilic acid disappeared rapidly. At the end of 32 weeks, less than 10% of applied arsanilic acid could be extracted from the soil. This compound degrades to arsenate and an unidentified organic moiety. Some formation of a volatile organic arsenical occurred in one soil used--Christiana soil. Degradation was more rapid under anaerobic then under aerobic conditions (Woolson, 1975).

CACODYLIC ACID (CA, DMAA) [Dimethylarsenic acid]

Using an aquatic ecosystem, ^{14}C-cacodylic acid was added to the soil, which was then flooded and allowed to incubate 7 days. During the first 30-50 days, ^{14}C increased in the water, plateaued and then declined. Algae and duckweed accumulated larger amounts of the carbon label than did any of the other components of the test system. Arsenic levels were highest in snails and crayfish. Daphnids and catfish showed no measurable accumulation of arsenic (Schuth et al., 1974).

When administered to rats, cacodylic acid was rapidly absorbed from the lung with a half-time of 2.2 min. Peroral absorption half-time was 248 min. The half-time for clearance from the whole blood after intravenous, intratracheal and peroral administration was 92, 76 and 90 days, respectively. In pregnant rats, cacodylic acid readily crossed the placenta. The small amount of $^{14}CO_2$ evolved indicated that only a small fraction of the dose was demethylated (Stevens et al., 1977).

It has been observed that molds grown in the presence of sodium cacodylate produced a garlic odor (Pool, 1912; Puntoni, 1917). This garlic odor has also been observed after addition of cacodylic acid to soil (Woolson and Kearney, 1973).

When the sodium salt of cacodylic acid was incubated with Penicillium brevicaule , trimethyl arsine evolved (Challenger and Higginbottom, 1935; Challenger et al., 1933). In other studies, when cacodylic acid was added to soil, volatile materials were identified by ion exchange and gas chromatography and mass spectroscopy as dimethylarsine and trimethylarsine. The monomethyl analog was not detected (Woolson, 1976 and 1977; Hiltbold, 1974). Microbial oxidation slowly released CO_2 and arsenate also (Hiltbold, 1974; Woolson and Kearney, 1973).

ARSENICALS

DSMA [Disodium methanearsonate]

Evolution of gaseous arsenic from DSMA-treated soil was a function of organic matter and moisture content. Greatest loss of arsenic was from soil containing 11% added organic matter and maintained under reduced conditions. The sorbed As was predominantly in the form of iron arsenate. Aluminum arsenate was the next most abundant form (Akins and Lewis, 1976).

Studies have identified the compound evolved from cultures of *Penicillium brevicaule* containing DSMA as trimethylarsine (Challenger and Higginbottom, 1933 and 1935).

ARSENICALS

MAA ([Magnesium ammonium arsenate]

Studies indicated that the ion of arsenious acid rather than the salt itself was the toxic principle (except with arsine gas). Reduction of MAA *in vitro* or *in vivo*, when combined with sodium sulfite, enhanced the toxicity of MAA to rats. The use of urea showed enhancement only *in vivo*. *In vitro* reduction of MAA by sulfur dioxide also enhanced MAA toxicity to roof rats (Bai et al., 1978).

ARSENICALS

MAF [Ferric methanearsonate]

When MAF was orally administered to rats, absorbed arsenic peaked in the blood at the fifth day. Urine and feces were sampled on the second day. TLC analyses indicated the presence of three major components which were identified as arsenic acid, DSMA, and DMAA. Arsenic acid, from urine, was identified by comparing its absorption spectrum in the AgDDC method with that of an authentic sample. The other two compounds, found in blood and urine, were identified by comparative GC-MS spectra. The biological half-life for arsenic in blood was 114 days. Most of the arsenic was deposited in organs and tissues and part in hair. The three major metabolites were also found in feces and kidney as well as the urine and blood (Odanaka, 1978a and b).

ARSENICALS

MSMA [Monosodium methanearsonate]

Wheat seedlings were treated with ^{14}C-MSMA at the 3-leaf stage. When harvested 3 months later, all parts of the plant contained radioactivity and 50% of the total ^{14}C in the seeds was present in a nonextractable bound form. Analysis indicated that this was in the form of unchanged ^{14}C-MSMA or conjugated to non-alcohol extractable lipid, nucleic acid and/or protein materials. Methyl arsine and a small amount of $^{14}CO_2$ were observed. These materials are released by soil degradation after root exudation of ^{14}C-MSMA into the soil (Domir et al., 1976a and b).

Over a 5-year period, MSMA was annually added to soil plots. Elemental arsenic did not increase in any plot receiving less than 36 kg/ha of MSMA. Significant arsenic residues were found in plots receiving 72, 144 and 288 kg/ha of MSMA for 5 years (Robinson, 1975).

When MSMA was added to soil, volatile gases were observed. These were identified by ion exchange and gas chromatography and mass spectroscopy as dimethylarsine and trimethylarsine. Monomethylarsine was not detected (Woolson, 1976 and 1977a and b; Hiltbold, 1974). Microbial oxidation slowly released CO_2 and arsenate also (Hiltbold, 1974).

A fungus and two actinomycetes, isolated from soil, degraded MSMA slowly and released CO_2 from ^{14}C-MSMA. TLC indicated the presence of arsenate in extracts from soil and microbial growth studies to which MSMA-^{14}C had been added (Von Endt et al., 1968).

ASULAM [Methyl 4-aminobenzenesulfonyl carbamate]

Asulam was applied to foliage of field bracken at the rate of 4.4 kg/ha. Evidence indicated that asulam was relatively persistent in the rhizome system. In the laboratory, 5 bracken plants were treated with ^{14}C-asulam and placed in a growth cabinet for 30 days. Analyses showed the presence of sulfanilamide, sulfanilic acid, 4-aminophenol, benzene sulfonamide and some unidentified material in addition to unchanged asulam. Residues on the surface, treated frond, and rhizome, were similar quantitatively. The major identified metabolite, sulfanilamide, varied from 6.3 to 8.3% whereas the unidentified material varied from 25.2 to 28.4%. The bulk of the label was recovered as unchanged asulam (59.1 to 62.0%). The other residues varied from 1.1 to 3.3% (Veerasekaran et al., 1976).

At soil temperatures of 20-35C and moistures above 50% of field capacity, asulam degradation approximated first-order kinetics. Degradation was rapid with a half-life of about 7 days (Smith and Walker, 1977).

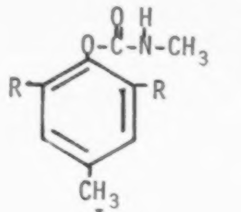
AZAK [2,6-Di-*t*-butyl-4-methylphenyl-*N*-methylcarbamate]

In this study of the photolysis of azak in ethanol, an attempt was made only to characterize products arising from β-cleavage (oxygen-carbon bond). Photolysis of azak (I) in aerated and degassed ethanol yielded 2,6-di-*t*-butyl-4-methylphenol (II), 3,5-di-*t*-butyl-1-methyl-4-oxo-2,5-cyclohexadiene-*N*-methylcarboxamide (III), and 2,5-di-*t*-butyl-3-methyl-6-hydroxy-*N*-methylbenzamide (IV). In degassed and aerated cyclohexane, photolysis of azak yielded only II. Similar results were observed in ethanol solution which was ca. 0.1 molar in piperylene.

Photolysis of the azak analog 2,6-di-*t*-butylphenyl-*N*-methylcarbamate (V) in aerated ethanol yielded 2,6-di-*t*-butylphenol (VI), 3,5-di-*t*-butyl-4-hydroxy-*N*-methylbenzamide (VII), and 2,5-di-*t*-butyl-6-hydroxy-*N*-methylbenzamide (VIII). In addition to IR, NMR, MS and UV spectra, the melting points and UV maxima were determined for the above compounds.

Photolysis of III in ethanol yielded I.

(Kumar et al., 1974)



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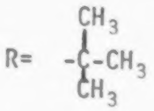

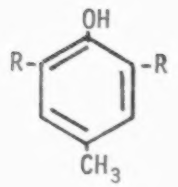

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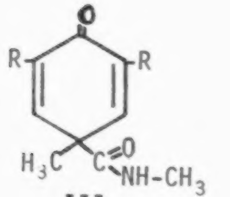

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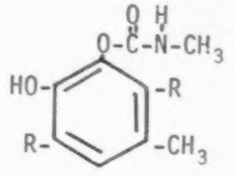

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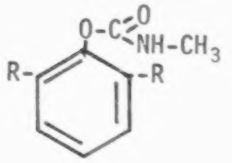

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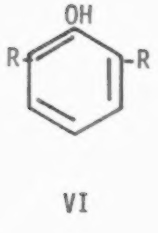

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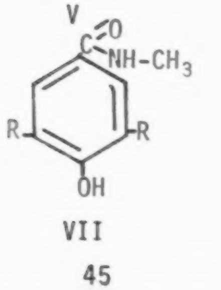
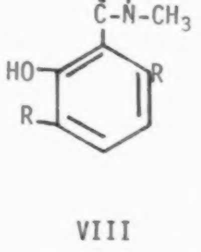


VII



VIII

AZINPHOSMETHYL (Methyl guthion) [*O,O*-Dimethyl S-(4-oxo-1,2,3-benzotriazin-3-(4H)-ylmethyl)phosphorodithioate]

In livers of male mice, azinphosmethyl was detoxified by glutathione dependent enzymes during inhibition of oxidative metabolism with piperonyl butoxide pretreatment. The oxon was not degraded by these enzyme systems (Levine and Murphy, 1977).

After 14 days exposure of bean plants (*Phaseolus vulgaris*) to ^{14}C-azinphos-methyl or -ethyl, 15 to 20% of the label was found in the water fraction and about 35% of this radioactivity was present in two of the more than 10 labeled compounds present. The radioactivity in the organic fractions was primarily (>90%) in the form of the original material (Wieneke and Steffens, 1974).

Field tests with azinphosmethyl indicated that on treated apple trees the half-life of this pesticide was about 2.6 to 6.3 days (Pree et al., 1976).

Studies on the photodecomposition of azinphosmethyl have shown that degradation, after an 8 h exposure to sunlight or ultraviolet light, was greatest on glass surfaces and variable on other surfaces.

Surface	Non-insecticidal water-soluble photoproducts formed (%)
Glass	18.6
Sandy soil	6.5
Muck	2.5
Corn leaves	3.5
Bean leaves	1.4

N-Methylbenzazimide was formed on corn leaves only. *N*-Methylbenzazimide sulfide (or disulfide), benzazimide and the oxygen analog of azinphosmethyl were formed on corn and bean leaves. Granular formulation was least susceptible to photodecomposition (Liang and Lichtenstein, 1976).

AZODRIN (Monocrotophos, Dimethyl *cis*-1-methyl-2-methylcarbamoylvinyl phosphate) [*O*,*O*-Dimethyl *O*-3-(*N*-methyl-*cis*-crotonamide) phosphate]

Most crops treated in the field contained no detectable residues of neutral conjugates of the *N*-hydroxymethyl metabolite. Occasionally, residues of 0.05 to 0.35 ppm were found in carrots, olives and oranges (Beynon et al., 1973).

BANAMITE [Benzoyl chloride (2,4,6-trichlorophenyl)hydrazone]

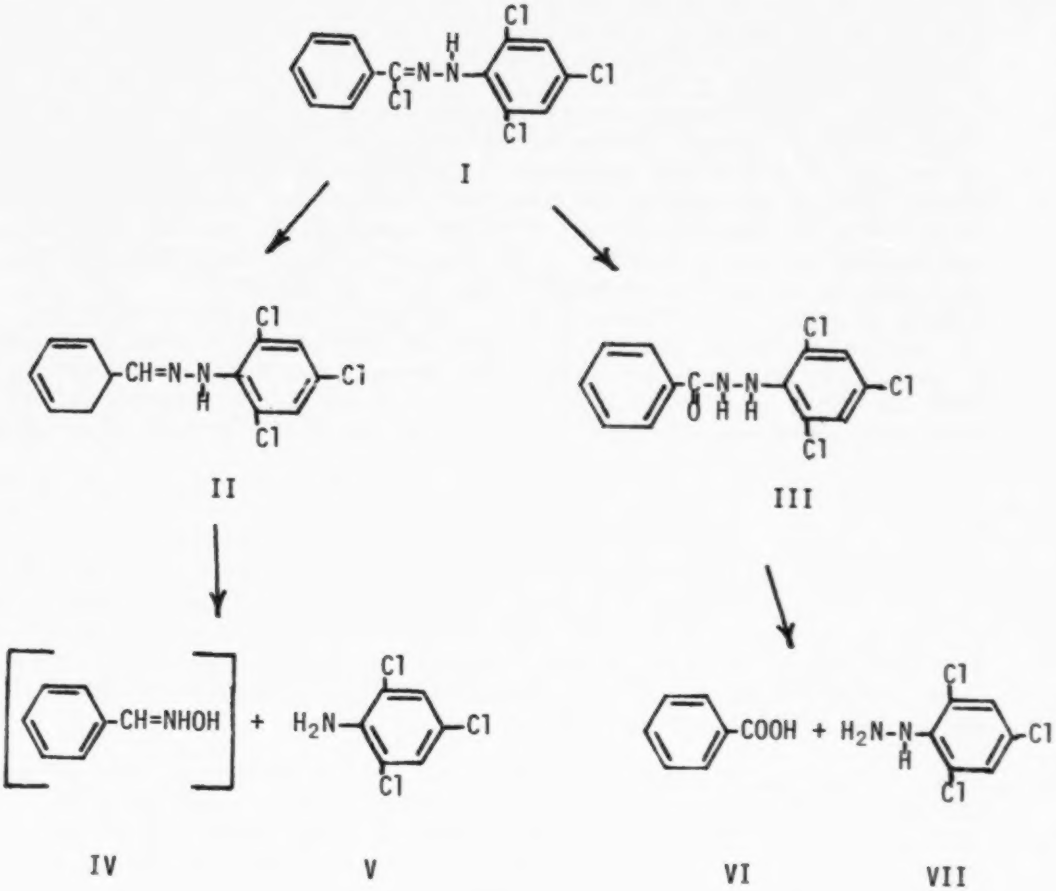
When the twospotted spider mite (*Tetranychus urticae* Koch) was exposed to Banamite, the major metabolites were identified as benzaldehyde 2-(2,4,6-trichlorophenyl)hydrazone (II) and benzoic acid 2-(2,4,6-trichlorophenyl)hydrazide (III). In addition to these, several unidentified metabolites and the following minor products were found: 2,4,6-trichloroaniline (V); 2,4,6-trichlorophenylhydrazine (VII); and benzoic acid (VI). Similar results were obtained with *in vitro* studies (see fig. I) (Knowles and Aziz, 1974).

In hexane, photolysis of banamite at 3500A produces *syn*-*anti* isomerization around the C=N double bond. This is the major reaction and the photoisomer reverts upon standing in the absence of light. When photolysis was conducted with a thin film on glass, the results were similar with 3500A bulbs, 3000A bulbs, and sunlight. The $t_{1/2}$ = 2 to 4 h. Analyses were conducted by TLC and GLC-MS. Products identified were :

II. benzoic acid (2,4,6-trichlorophenyl)hydrazide
III. *N*,*N*'-dibenzoyl-*N*-(2,4,6-trichlorophenyl)hydrazine
IV. 2,4,6-trichlorobenzanilide
V. N,*N*'-dibenzoyl-N-(2,4-dichlorophenyl)hydrazine
VI. 2,4,6-trichlorobenzophenone
VII. 2,4-dichlorobenzophenone
VIII. 3,6-diphenyl-2,5-bis(2,4,6-trichlorophenyl)-2,5-dihydro-*s*-tetrazine
IX. 3,5-diphenyl-1-(2,4,6-trichlorophenyl)-1,2,4-triazole
X. 4,5-diphenyl-2-(2,4,6-trichlorophenyl)-1,2,3-triazole
XI. 2,2',4,4',6,6'-hexachloroazobenzene

In a field application of banamite to an orange tree, compounds VIII and IX were observed as residues on the leaves (Friedman et al., 1974).

Figure I


Cl
C=N-N
H
Cl
I
CH=N-N
H
II
C-N-N
O H H
III
CH=NHOH
+
H₂N
IV
V
COOH
+
H₂N-N
H
VI
VII

BAY NTN 9306 [O-Ethyl O-(4-methylthiophenyl) S-propyl phosphorodithioate]

^{14}C-Labeled Bay NTN 9306 was administered orally in feed with a balling gun to a lactating Jersey cow. In 6 days posttreatment, 90% of the radiocarbon appeared in the urine, 13% in feces and 0.1% in milk. TLC indicated the presence in urine of at least 18 metabolites. Most of the radiocarbon in the urine was in the form of phenol sulfide, sulfone and/or sulfoxide and was present both free and conjugated. Feces contained phenol sulfoxide and the sulfoxide of Bay NTN 9306 as well as unmetabolized material. The major metabolites in milk were phenol sulfone and sulfoxide, free and conjugated. In addition there were traces of phenol sulfide, free and conjugated, and the sulfoxide and sulfone of Bay NTN 9306. Some unextractable radiocarbon residues were present as well as unmetabolized starting material. Liver and kidney were the only tissues containing sufficient labeled material for analysis. Major metabolites were the sulfide, sulfoxide and sulfone of phenol in both free and conjugated forms. The sulfone of Bay NTN 9306 was found in liver but not kidney. In addition to unmetabolized material, there were five unidentified metabolites (Ivie et al., 1976a).

In white female rats, Bay NTN 9306 was metabolized rapidly after oral administration. TLC analyses of urine indicated the presence of the phenol sulfide, sulfoxide and sulfone conjugated probably as glucuronides and sulfates. Also present in trace amounts were the sulfoxide and sulfone of Bay NTN 9306. Tissues contained the sulfoxide of the oxon analog as well as Bay NTN 9306 and its sulfoxide and sulfone and the sulfoxide and sulfone of phenol. Bay NTN 9306 oxon and oxon-sulfone were identified by TLC only. Other metabolites were identified by TLC and GLC-MS (Bull and Ivie, 1976).

After foliar application of Bay NTN 9306 to cotton plants, the following metabolites were found on and in the cotton leaves: Bay NTN 9306 sulfoxide and sulfone; Bay NTN 9306 oxon sulfone; phenol sulfoxide and sulfone; and glucosides of phenol sulfide, phenol sulfoxide and phenol sulfone. Similar results were obtained in a soil study. In an artificial pond, 50% depletion of radioactivity was reached after 75 days; but after 2 h only half the radioactivity was in the parent form. The principal product was phenol sulfoxide through day 16. Phenol sulfone and the sulfoxide and sulfone of Bay NTN 9306 were also observed (Bull et al., 1976).

On cotton leaves, ^{14}C-labeled 9306 degraded rapidly in sunlight. Less than 20% of the deposit remained after 2 days exposure. Results of these studies and those done with exposure on glass surfaces or in water solutions are summarized.

Bay NTN degradation after sunlight exposure

Metabolite	On Cotton Leaves	On Glass Surface	In Water
Bay NTN 9306 sulfoxide	++	++	++
Bay NTN 9306 sulfone	++	++	+
Oxon-sulfone	+	+	-
Phenol	+	+ (<1%)	+
Phenol sulfoxide	+	+	++
Phenol sulfone	+	+	+
Unknown 1	+	+	+
2	++	++	++
3			+
4	+ (<1%)		+
5			+ (<1%)
6	+		+
7			+
8	+	+	
9		+	
10		+ (<1%)	
11	+ (<1%)		
12	+ (<1%)		

(Ivie and Bull, 1976)

BAYER 73 (Bayluscide) [2-Aminoethanol salt of 2',5-dichloro-4'-nitrosalicylanilide]

BAYER 2353 (Niclosamide) [2',5-Dichloro-4'-nitrosalicylanilide]

In rainbow trout (Salmo gairdneri) exposed to ^{14}C-labeled Bayer 73 in water, depuration apparently occurred within 72 h. Biliary concentration was high, reaching a 10,000:1 bile to water ratio in 24 h. Analyses indicated that the metabolite in bile was the glucuronide (Statham and Leach, 1975). Preliminary studies also indicated that fish were capable of hydrolysis of Bayer 73 to 5-chlorosalicylic acid and 2-chloro-4-nitroaniline (Allen et al., 1978). In rats orally administered Bayer 73, the main metabolite observed in urine was identified as the amino analog by UV and thin-layer analyses (Duhm et al., 1961).

When midge larvae (Chironomus tentans) were exposed to sublethal concentrations of ^{14}C-Bayer 2353, ^{14}C-residues accumulated rapidly and were directly related to water hardness and amount of toxicant present. Excretion was rapid. Metabolism of this material produced an unidentified compound and ^{14}C-chlorosalicylic acid (Kawatski and Zittel, 1977).

The metabolism of niclosamide was studied with intact worms (Ascaris lumbricoides var. suum and Monieza expansa). Hydrolysis of the amide bond was not observed. However, the nitro group was reduced. The corresponding amine was identified by TLC co-chromatography. Tissue preparations were also prepared from these worms. With A. lumbricoides var. suum, only the intestinal brush border epethelial cells reduced niclosamide and the nitro-reductase appeared to be in the cytosol of these cells. The enzymes from both worms exhibited pH optima of 6.4 to 6.6 for niclosamide reduction. Enzyme preparations from mouse and sheep livers also reduced niclosamide to the corresponding amine. These preparations did not hydrolyze the amide bond (Douch and Gahagan, 1977).

In other studies, concentrated solutions of Bayluscide began to lose activity within 48 h after inoculation with bacterial isolates obtained from snail-culture water in which Australorbis glabratus (Puerto Rico strain) had been maintained for one week (Etges et al., 1965).

Bayer 2353 exhibited no hydrolysis in pond water or in distilled water buffered at pH 5.0, 6.9 or 8.7 after 56 days. However, degradation of 2353 was rapid when exposed to UV on silica gel TLC plates and on glass slides. Less than 50% of the Bayer 2353 remained after 24 h and after 168 h there was less than 5% of the parent material. In aqueous solution, after 14 days of exposure to long-wave UV, only 5% of the remaining material was the original compound (Schultz and Harman, 1978).

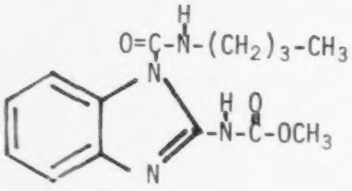
BENOMYL (Benlate, Dupont F-1991) [Methyl N-(N-butylcarbamoyl-2-benzimidazolyl)carbamate]

CICLOBENDAZOLE [Methyl N-(5-cyclopropylcarbonyl-2-benzimidazole) carbamate]

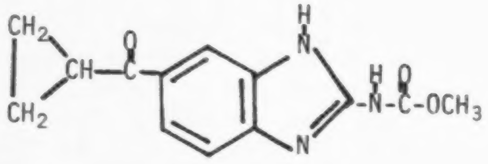
FENBENDAZOLE (Panacur) [Methyl N-(5-phenylthiobenzimidazol-2-yl) carbamate]

MBC (Carbendazim) [Methyl N-(2-benzimidazolyl)carbamate]

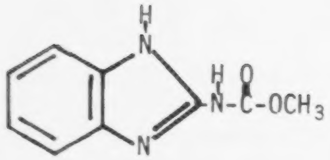
THIOPHANATE-METHYL (Th-M, TPM) [1,2-Bis(methoxycarbonylthioureido) benzene]



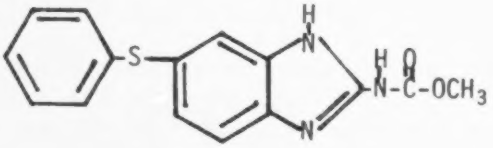
Benomyl



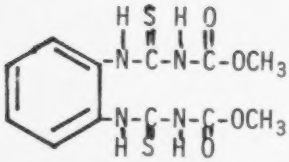
Ciclobendazole



MBC



Fenbendazole



Thiophanate-Methyl

BENOMYL [Methyl N-(N-butylcarbamoyl-2-benzimidazolyl)carbamate]

Rats were fed 2500 ppm benomyl in the diet. Urine was collected and analyzed. Chromatography and IR were used to identify the major metabolite as the glucuronide and sulfate of 5-hydroxy-2-benzimidazolecarbamate (5-HO-MBC). A small amount was present unconjugated (Gardiner et al., 1968).

Application of benomyl to carrots, strawberries and apples at normal rates gave rise to low concentrations of MBC, free and conjugated; 2-AB, free and conjugated; and benzimidazole, 2-aminobenzonitrile, and o-phenylendiamine as free compounds (Rouchaud et al., 1977a).

Melon plants (Cucumis melo) were treated with benomyl, 2-aminobenzimidazole (2-AB), or benzimidazole (BZ) in a growth medium. Analyses of leaves of melon plants showed that benomyl gave rise to MBC (or Carbendazim), 2-AB, BZ, 2-aminobenzonitrile, o-phenylenediamine, and aniline in the free state; to MBC, 2-AB and BZ in a bound form. Treatment with 2-AB gave the same products as with benomyl except for MBC, free and bound; and results with BZ treatment gave all products derived from 2-AB (Rouchaud et al., 1977b).

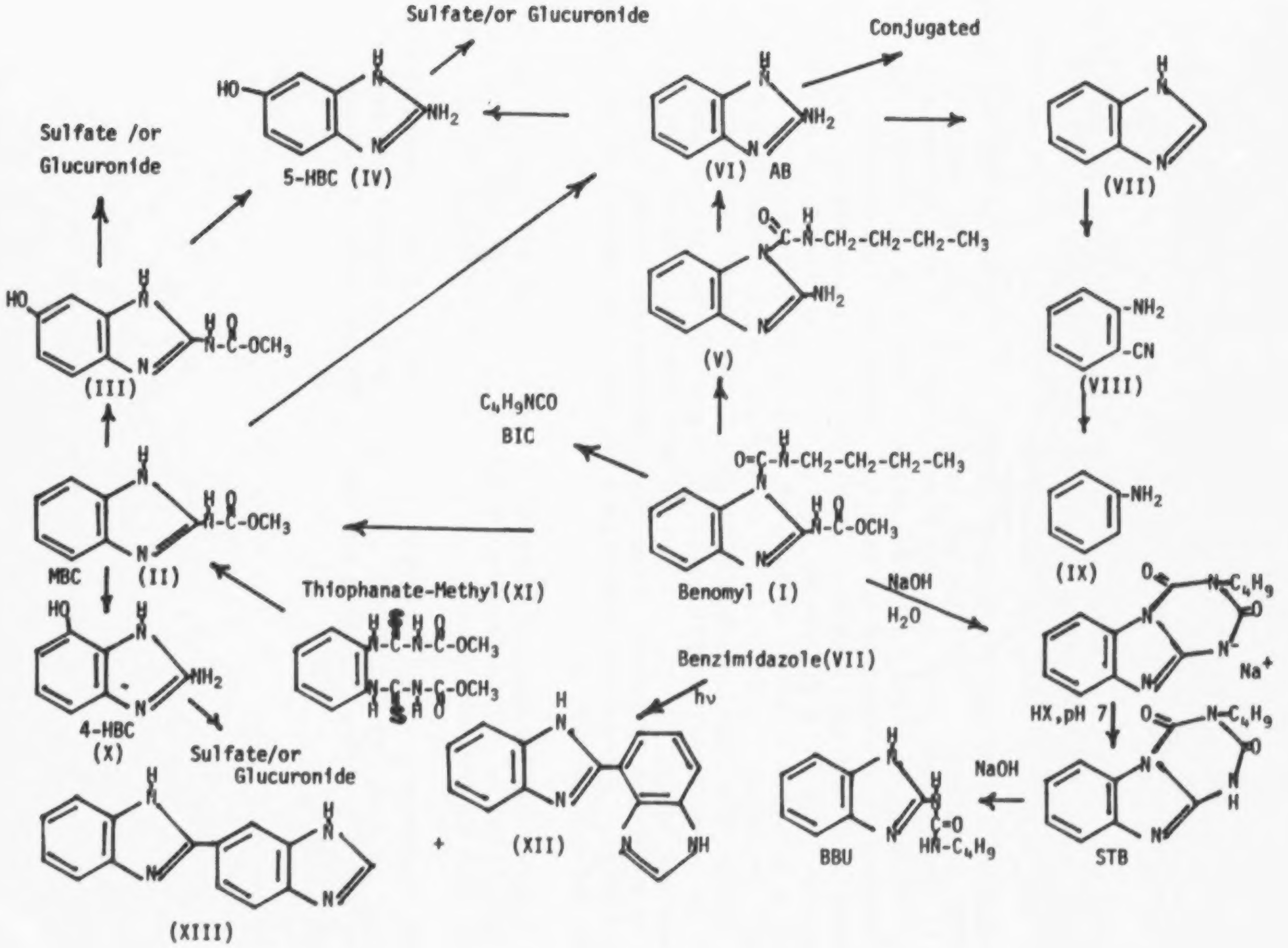
When applied to bananas, benomyl was retained mainly on the skin. No 2-AB was detected. The UV residue procedure used converted benomyl to MBC and analyses were not specifically made for the latter (Cox and Pinegar, 1976).

When benomyl was applied to pruned apricot sapwood, fungitoxicant recovered varied between 45 and 15% after 15 days. TLC indicated that the material recovered was MBC (Price and Carter, 1975).

Benomyl was dissolved in nutrient solution in which bean plants were grown. After one day, only MBC was recovered from the solution. MBC was also recovered from leaflets after 7 days (Peterson and Edgington, 1970). Similarly, MBC was observed in tomato plants treated with benomyl (Peterson and Edgington, 1971).

When pear trees were sprayed with benomyl, the average rate of degradation was 4% per 10 days. The residue level of MBC in the leaves was 50 ppm after 4 days and 8 ppm after 7 months. A metabolite identified as 2-aminobenzimidazole (2-AB) was also present in small amounts (Ben-Aziz and Aharonson, 1974).

Four strains of bacteria and two fungi were obtained from soil that were capable of degrading benomyl. Products were not identified (Helweg, 1972). In other studies, using water and soil samples, a large number of microorganisms were isolated which were capable of


Sulfate/or Glucuronide
Conjugated
Sulfate /or Glucuronide
5-HBC (IV)
(VI) AB
(VII)
(III)
(V)
(VIII)
C_4H_9NCO
BIC
MBC
(II)
Benomyl (I)
(IX)
NaOH
H_2O
Thiophanate-Methyl(XI)
Benzimidazole(VII)
hν
Na^+
4-HBC
(X)
Sulfate/or Glucuronide
HX,pH 7
NaOH
BBU
STB
(XII)
+
(XIII)

using benomyl as a sole source of carbon. Most of these organisms were *Pseudomonas* spp. It was believed that *n*-butylamine, split nonenzymatically from the butylcarbamoyl side chain, was the actual carbon source for these microorganisms. The MBC formed by this hydrolysis was degraded to 2-AB. Pure cultures did not cleave the benzimidazole nucleus (Fuchs and de Vries, 1978a). Using 2-^{14}C-labeled MBC, the nonenzymatic hydrolytic product of benomyl, studies with mixed cultures showed the formation of $^{14}CO_2$ and the cleavage of the benzimidazole nucleus. A compound, not fully characterized, was observed that exhibited UV spectra similar to that of 2-AB and was believed to be a 2-AB nucleotide (Fuchs and de Vries, 1978b).

Hydrolysis of benomyl in water was progressive with time and gave rise to methyl benzimidazole carbamate (BCM). Both benomyl and BCM were strongly adsorbed to loam (Fuchs et al., 1970).

An investigation of the kinetics of benomyl conversion to MBC indicated a pseudo-first order. Over the pH range 2.5 to 7.0, the reaction rate is independent of pH and the final product is MBC (Calmon and Sayag, 1976a). In mildly alkaline media, conversion of benomyl to STB involves an elimination to form the isocyanate intermediate followed by a fast cyclization. In strongly alkaline media, this conversion occurs via a dianion. At pH 13.5 the conversion of STB to BBU occurs and is first order with respect to hydroxide ion (Calmon and Sayag, 1976b). In 14 solvents studied, formation of MBC from benomyl proceeded via spontaneous intramolecular catalysis and exhibited no correlation with existing empirical solvent parameters (Calmon and Sayag, 1976c). Except in methanol and ethanol, BIC addition to solutions of benomyl stabilized degradation to MBC (Chiba, 1975; Chiba 1977a). Increasing temperature increased decomposition of benomyl to MBC and BIC (Chiba, 1977b).

When benomyl and Bordeaux mixture were mixed, a compound was formed that was identified as *s*-triazino-benzimidazole (STB). The same compound was formed when benomyl was placed in solution of pH 12 (Ogawa et al., 1971).

Benomyl hydrolysis to MBC was rapid in methanol and ethyl acetate with a $t_{1/2}$ = <1 h at low concentrations. At high concentrations, benomyl was relatively stable in $CHCl_3$ and CH_2Cl_2 (Chiba, 1975; Chiba and Cherniak, 1978).

CICLOBENDAZOLE [Methyl N-(5-cyclopropylcarbonyl-2-benzimidazole) carbamate]

Adult CFY rats and beagle dogs were given ciclobendazole orally as a suspension in propylene glycol or i.v. as a solution in propylene glycol. Feces, urine and bile were collected and analyzed. Bile of rats contained the 6-hydroxy analog as a conjugate. This compound was also excreted as a conjugate in dog and rat urine and free in rat bile, rat urine and to a lesser extent in rat feces. With dogs, the 6-hydroxyciclobendazole was not found in dog bile or fecal extracts and appeared in dog urine as a minor metabolite. Some 5-cyclopropylcarbonyl-2-aminobenzimidazole was formed in the rat and excreted in the urine. Dog bile also contained some 5-(α-hydroxycyclopropylmethyl)-2-aminobenzimidazole. This compound was not found in rat or dog urine or fecal extracts (Mayo et al., 1978).

FENBENDAZOLE (Panacur) [Methyl N-(5-phenylthiobenzimidazol-2-yl) carbamate]

Fenbendazole was administered to cattle, sheep, and pigs. Between 44 and 50% of the dose was excreted unchanged in feces and about 0.1% in urine. The main metabolites were identified as the 4-hydroxyphenylthio analog and 2-amino-5-phenylthiobenzimidazol. In addition to these, two others were observed in pig urine (Düwel, 1977).

MBC (Carbendazim) [Methyl *N*-(2-benzimidazolyl)carbamate]

2-^{14}C-labeled MBC was applied to strawberry (*Fragaria ananosa* 'Superfection') plants. MBC was metabolized more rapidly than in other plants. 2-AB, the only metabolite identified, was present in foliage and roots. Other unidentified compounds were observed. Studies with β-glycosidase, glucuronidase, sulfatase, and acid and NaOH treatment, indicated the formation of *N*- and/or *O*-conjugates of MBC and 2-AB with glucose and hemicelluloses (Siegel, 1973).

After exposure of *Aspergillus nidulans* to MBC, the 5-hydroxy analog was identified as a metabolite. This was further metabolized but the product was not identified (Davidse, 1976).

The effect of MBC on mycelial growth of *A. nidulans* was positively correlated with affinity of the binding sites of fungal tubulin for MBC. Binding constants for MBC varied from 3.7×10^4 (a resistant strain), and 4.5×10^5 (a wild strain), to 1.6×10^6 l/mol (sensitive strain) (Davidse and Flach, 1977).

Increasing soil acidity increased adsorption of MBC. This was ascribed to ionization at lower pH values and adsorption of ionized molecules. After 9 months, 65-75% of MBC applied to soil was recovered from air dried soils; 20-30%, from moist soil (Aharonson and Kafkafi, 1975a and b).

^{14}C-MBC was degraded in soil with evolution of $^{14}CO_2$. Similarly, ^{14}C-2-AB, a degradation product of MBC, was degraded to $^{14}CO_2$ (Helweg, 1978).

After exposure of MBC on silica gel G to sunlight for 30 h, more than 90% of MBC was recovered. Presence of riboflavin or acetone increased loss. The predominant reaction observed was rupture of the benzene ring of MBC. Photooxidation products found were: guanidine, carbomethoxyguanidine, dicarbomethoxyguanidine, carbomethoxyurea, 2-AB and CO_2. After MBC was applied to leaves of corn plants and then exposed to sunlight for 18 h, no photolysis products were found in plant extracts (Fleeker and Lacy, 1977).

MBC was exposed on glass plates to sunlight. A change occurred slowly. Then MBC was exposed in MeOH to UV irradiation for 4 days. Analyses showed the presence of dimethyl oxalate, an acid salt of guanidine and some unidentified material (Watkins, 1974).

THIOPHANATE-METHYL (Th-M, TPM) [1,2-Bis(methoxycarbonylthioureido) benzene]

The conversion of thiophanate-methyl (TPM) was accelerated by thin potato slices, homogenates of apple and potato, and the sap of cucumber seedlings. Although no direct proof was given, it was suggested that the *o*-quinones generated in the plant tissues were the catalysts for conversion of TPM to MBC (Vonk et al., 1977).

Mycelia of the fungi *Pellicularia sasakii* (Shirai) S. Ito, sensitive to TPM, and *Alternaria mali* Roberts, insensitive to TPM, were exposed to ^{14}C-thiocarbonyl-labeled TPM. The main metabolite was identified as MBC and a minor metabolite as methyl 5-hydroxy-2-benzimidazolecarbamate (5-OH-MBC). Another metabolite was observed but not identified. The latter was formed only by the sensitive fungi (Yasuda et al., 1973).

In aqueous dispersion, thiophanate-methyl is stable between pH 1 to 9. Similarly, no spectral changes were observed after seven days in chloroform, methanol or a mixed solvent of $CHCl_3$ + CH_3OH + 0.1N HCl (1+4+1 by volume). When thiophanate-methyl was dissolved in ethyl acetate, spectral changes occurred which were coincidental with the disappearance of the thiophanate-methyl spectrum and appearance of the MBC spectrum (Courtney, 1977).

BENTAZON (Basagran) [3-Isopropyl-1H-2,1,3-benzothiadiazin(4)-3H-one-2,2-dioxide]

In animals, dietary bentazon was excreted as 6- and 8-hydroxybentazon conjugates (Kupelian, 1975).

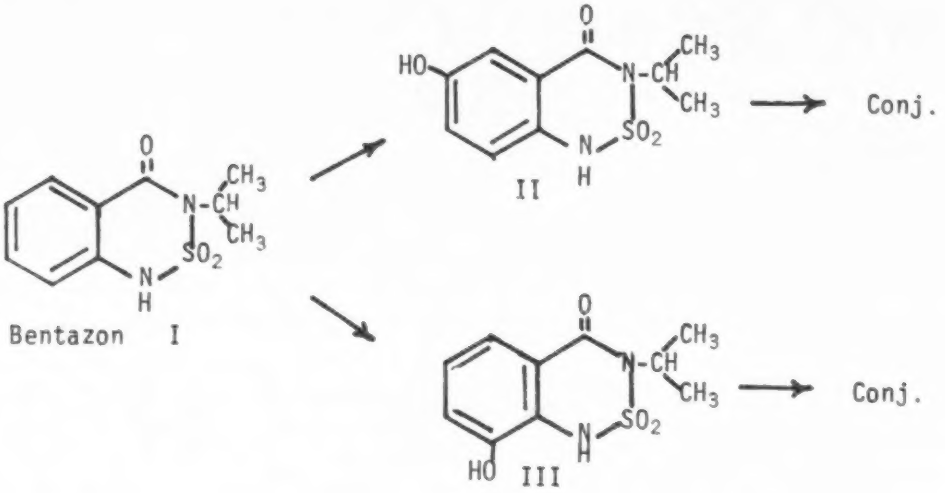
In studies with soybeans [*Glycine max* (L.) Merr.] and navy beans (*Phaseolus vulgaris* L.), four unidentified conjugates were observed (Mahoney and Penner, 1975). After foliar or root absorption, bentazon was rapidly metabolized by soybeans with hydroxylation at the 6- and 8- position. These were conjugated (Kupelian, 1975). Analysis of soybean field samples showed hydroxylation of bentazon in early growth stages (Cannizzaro, 1975).

Although absorption and translocation of bentazon was not markedly different in resistant rice and susceptible *C. serotinus*, metabolism differed markedly. In rice, there was 80% metabolism of absorbed bentazon within 24 h and 85% conversion to a major water-soluble metabolite within 7 days. In *C. serotinus*, there was only 25-50% metabolism of bentazon in 7 days. Similar results were obtained with other resistant and susceptible plant species indicating that ability to metabolize this compound is the primary mechanism of selectivity. The primary metabolite in rice was identified by GC-MS, NMR and IR as 6-(bentazon)-*O*-β-glucopyranoside (Mine et al., 1975). Other studies showed that the 6- and 8-hydroxybentazon were formed in about equal amounts in soybeans and that the 6-hydroxy analog predominates in wheat, rice, peanuts, *Senecio* sp., and *Chenopodium* sp. (Otto, 1975; Retzlaff and Hamm, 1976).

In cultivated plants studied, the 6- and 8-hydroxybentazons formed mono- and oligosaccharides (Otto et al., 1978).

Photolysis of bentazon in water for 115 h with 3000-3500 Å lamps produced compounds IV, V, VI, VII, VIII, IX, X and XI. The latter four are postulated structures most consistent with all data. Similar results were observed with a methanol-water solvent system. Photolysis of bentazon in sunlight as an aqueous solution in a sealed pyrex vessel gave compounds IV, VI, VIII, IX, X and XI. When irradiated on Montcalm sandy loam, bentazon gave compounds V, VI, VIII, IX, X and XI. When a thin film of bentazon on pyrex was used, only products IV, V and VI were observed (Nilles and Zabik, 1975).

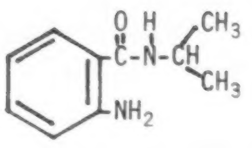
The aromatic ring of bentazon was hydroxylated in soil (Kupelian, 1975). At concentrations of 2 to 10 ppm, bentazon $t_{1/2}$ = 2 to 5 weeks in soil. The hydroxybentazons could not be detected, possibly because they were immediately incorporated into the humic substances and fulvic acids (Otto et al., 1978). When soil was treated with bentazon, the major metabolite identified was 2-amino-*N*-isopropyl benzamide (Butts, 1976).



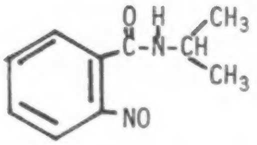
Bentazon I

II

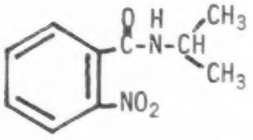
III



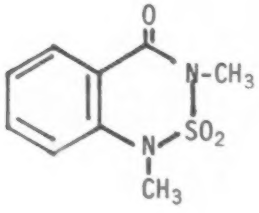
IV



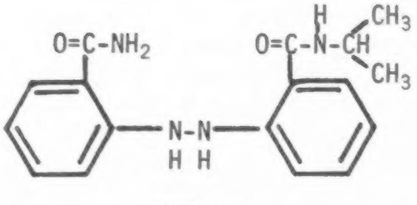
V



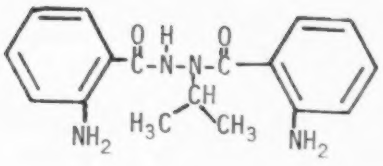
VI



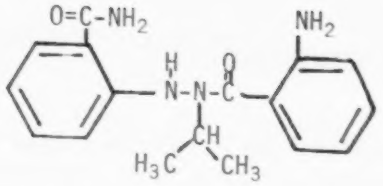
VII



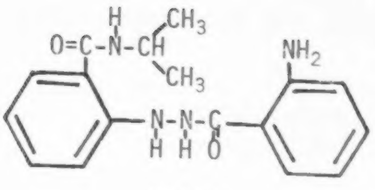
VIIIa


O H O
C-N-N-C
CH
H3C CH3
NH2
NH2

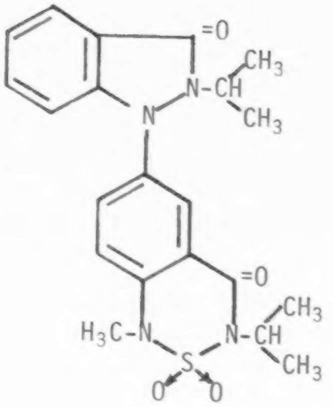
VIIIb


O=C-NH2
NH2
H O
N-N-C
CH
H3C CH3

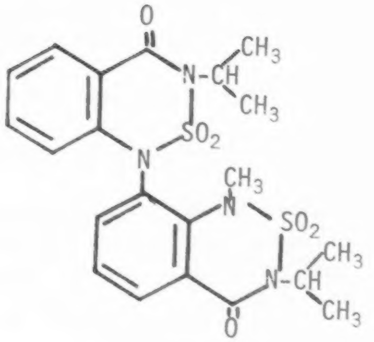
VIIIc


H CH3
O=C-N-CH
CH3
NH2
N-N-C
H H O

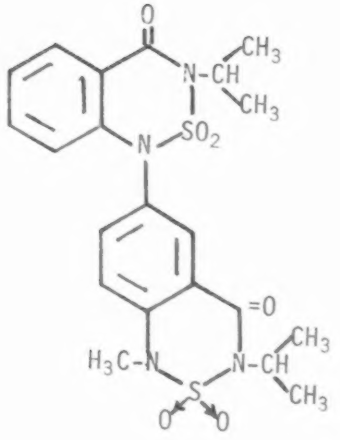
VIIId


=O
N-CH
CH3
CH3
N
=O
H3C-N
N-CH
CH3
CH3
S
O O

IX


O
N-CH
CH3
CH3
SO2
N
CH3
N
SO2
N-CH
CH3
CH3
O

X


O
N-CH
CH3
CH3
N
SO2
=O
H3C-N
N-CH
CH3
CH3
S
O O

BENZANILIDES

Benzanilide fungicides were incubated with *B. sphaericus* and with enzyme preparations. Compounds tested were hydrolyzed by both and produced aniline and the respective benzoic acid analog. Degradation rates for whole cells followed the order:

2-F>Benzanilide>2-Cl>2-CH_3>2-Br>2I.

(Engelhardt and Wallnofer, 1976a)

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BENZOYLPROP-ETHYL (Suffix) [N-(3,4-Dichlorophenyl)-N-2-(ethyl propionate)benzamide]

FLAMPROP-ETHYL [N-(3-Chloro-4-fluorophenyl) N-2-(ethyl propionate) benzamide]

FLAMPROP-METHYL (Mataven) [N-(3-Chloro-4-fluorophenyl) N-2-(methyl propionate)benzamide]

FLAMPROP-ISOPROPYL (Barnon) [N-(3-Chloro-4-fluorophenyl) N-2-(isopropyl propionate)benzamide]

When benzoylprop-ethyl or flamprop-methyl were fed to lactating cows, residues in milk were generally below 0.001 mg/kg and less than 0.003 mg/kg in muscle tissue. Residues of flamprop-isopropyl in milk and muscle of cows were similar. Residues in hen eggs were about 0.0008 mg/kg. Elimination of residues was rapid after treatment was stopped. The major metabolite in each case seemed to be the corresponding acid resulting from de-esterification (Crayford et al., 1976).

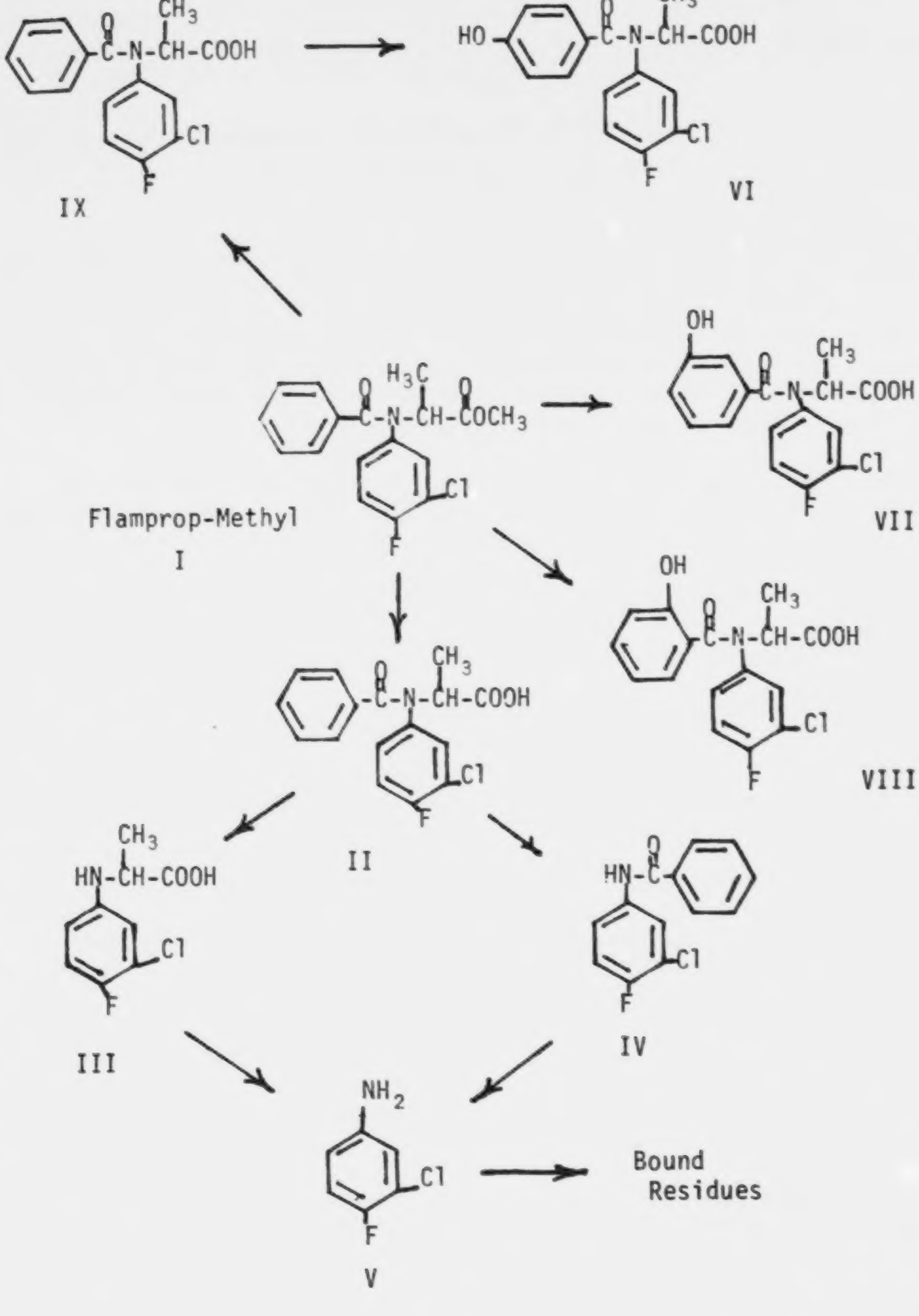
Wild oat (Avena fatua L.) in hydroponic culture was treated with benzoylprop-ethyl. These studies indicated that increased herbicide efficacy was brought about by reduced light and nutrients which resulted in higher levels of benzoylprop acid (Hill and Stobbe, 1978). A carboxylesterase, not present in wheat (Triticum aestivum L.), was prepared from wild oat. This enzyme was capable of deesterification of benzoylprop-ethyl to the acid (Hill, 1978; Hill et al., 1978).

Flamprop-methyl was applied to spring wheat and studied under glasshouse and outdoor conditions. The carboxylic acid was the major product found. Other metabolites included the glucuronide, 3'-chloro-4'-fluorobenzanilide, and the 3-HO- and 4-HO- analogs of flamprop-methyl (Roberts, 1977a).

When stored in soil under anaerobic conditions, flamprop-methyl was converted primarily to the carboxylic acid derivative (II). In addition to the 2-, 3-, and 4-hydroxybenzoyl analogs of II, another compound was identified as N-benzoyl-N-(3-chloro-4-hydroxyphenyl)-2-aminopropionic acid (Roberts and Standen, 1978).

When flamprop-isopropyl was orally administered to dogs and rats, 90% of this compound was excreted in the feces by male rats, 76.3% by female rats, and 53% by dogs. Metabolites II-XIII were identified with co-chromatography and MS (Hutson et al., 1977).

Rats and beagle dogs were administered flamprop-isopropyl. The major metabolite in urine and feces was the acid (V). TLC and GC-MS were


IX
VI
Flamprop-Methyl
I
VII
VIII
II
III
IV
V
Bound Residues

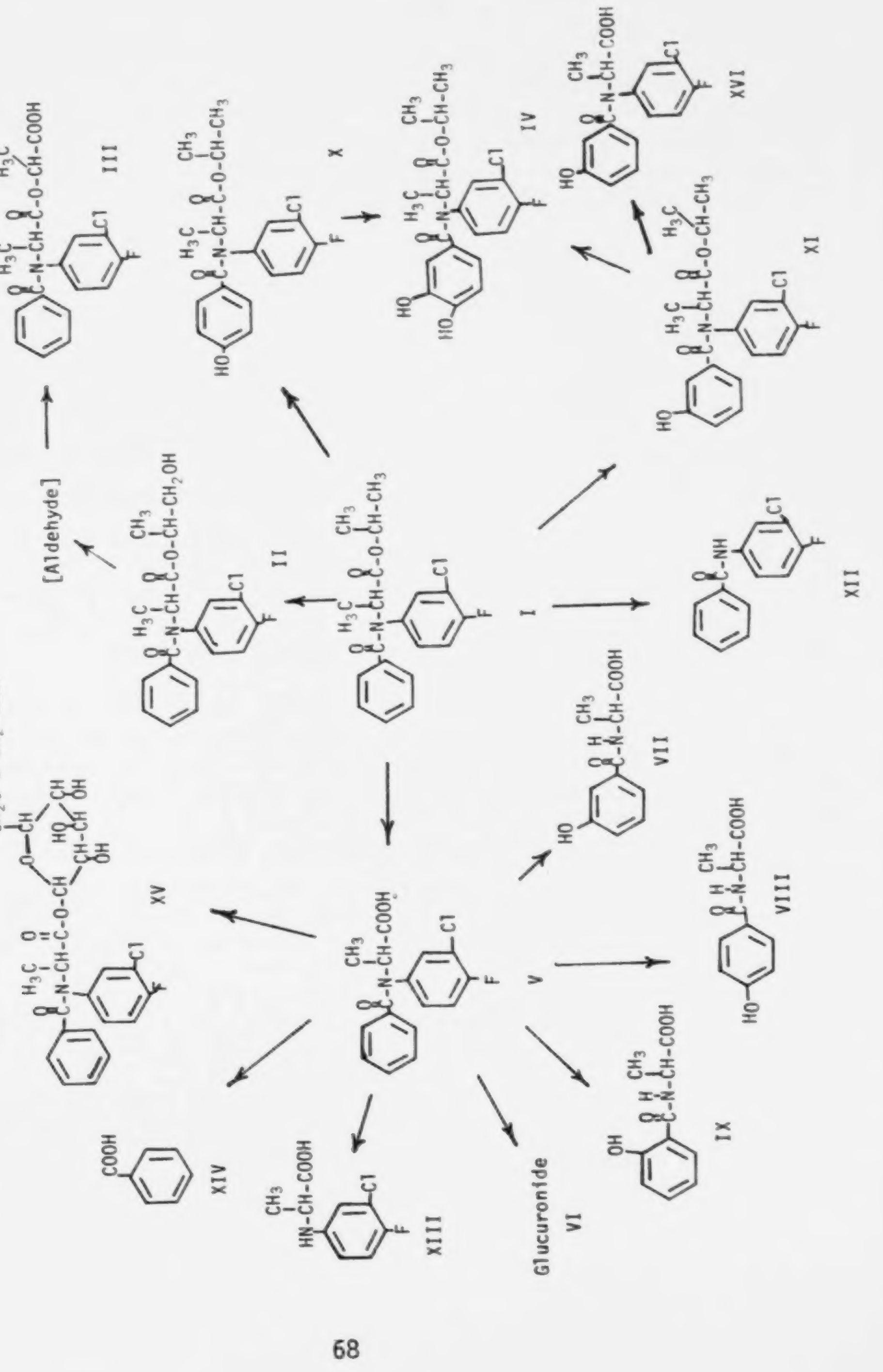
used to identify compounds II and III. Hepatic microsomal preparations also de-esterified flamprop-isopropyl. There was also a strong suggestion by these studies that hydroxylation of C-2 of the isopropyl group occurred with rapid spontaneous breakdown to compound XII (Bedford et al., 1978).

When flamprop-isopropyl was applied to barley, seven metabolites were observed and identified: compounds V, VII, VIII, X, XII, XIII and XIV. The soil contained the carboxylic acid (V), as well as some unidentified polar material (Roberts, 1977b). In other studies, it was found that flamprop-isopropyl conversion to the acid was necessary for biological activity (Jeffcoat and Harries, 1975).

In wild oats treated with flamprop-isopropyl, hydrolysis of the ester gave the corresponding acid (V). This was observed free and conjugated. Other compounds identified included: N-benzoyl-3-chloro-4-fluoroaniline (XII); 2-(3-chloro-4-fluorophenylamino)propionic acid (XIII); benzoic acid (XIV); 4-hydroxybenzamide analog (X); 3-hydroxybenzamide analog (XI); and 3-hydroxybenzamide analog of the free acid (XVI). In addition to these, metabolites V, XIV, X, XI, and XVI were also present as conjugates, not further defined (Roberts, 1977b).

Using abscissed wheat seedlings that were maintained in a flamprop solution, large amounts of a conjugate were formed. After isolation, MS was used to characterize the metabolite as a malonyl glucopyranoside of the free acid (XV). The malonyl group is believed to be joined to the hexose at the 6-position (Dutton et al., 1976).

Moderately alkaline hydrolysis of flamprop esters produced the corresponding acids and alcohols. When conducted under more basic conditions, hydrolysis of the ester was followed by cleavage of the amide bond to give benzoic acid and the N-phenyl substituted amino acid. In strong acid media, deesterification was followed by production of the corresponding aniline (Brown, 1978).


I
II
III
IV
V
VI
VII
VIII
IX
X
XI
XII
XIII
XIV
XV
XVI
[Aldehyde]
Glucuronide

BHC (Benzene hexachloride, HCH) [1,2,3,4,5,6-Hexachlorocyclohexane]

Lindane = γ-isomer of BHC

The urine of men occupationally exposed to HCH were analyzed for residues. GC with four different columns were used for identification. The α-, β-, γ-, and δ-isomers were identified in addition to the following metabolites which were in the free state:

hexachlorobenzene (HCB)
γ-pentachlorocyclohexene (γ-PCCH)
δ-pentachlorocyclohexene (δ-PCCH)
pentachlorobenzene (PCB)
pentachlorophenol (PCP)
2,3,4,5-tetrachlorophenol (2,3,4,5-TeCP)
2,3,4,6- and/or 2,3,5,6-tetrachlorophenol (2,3,4,6- and/or 2,3,5,6-TeCP)
1,2,3,4-tetrachlorobenzene (1,2,3,4-TeCB)
2,4,6-trichlorophenol (2,4,6-TCP)
2,4,5- and/or 2,3,6- and/or 2,3,5-trichlorophenol

The following were observed as glucuronide conjugates:

2,3,4,6- and/or 2,3,5,6-tetrachlorophenol
2,4,6-trichlorophenol
pentachlorophenol
2,3,4,5-tetrachlorophenol
2,3,4-trichlorophenol
other trichlorophenols not further identified

(Engst et al., 1976b and c)

After administration of lindane to male Wistar rats by gavage, tissues and excreta were analyzed. Lindane was excreted in urine unchanged in large amounts and PCP, 2,3,4,6-/or 2,3,5,6-TeCP, 2,4,6-TCP, γ-PCCH, and tetrachlorocyclohexenol (TeCCOL) were detected. Feces contained only lindane. PCP, 2,3,4,5-TeCP, 2,3,4,6-/or 2,3,5,6-TeCP, and 2,3,5-/or 2,3,6-/or 2,4,5-/or 3,4,5-TCP were present to a small extent as β-glucuronides in addition to the free form. Results of this study and the feeding of other potential HCH metabolites are summarized in the following table (Engst et al., 1976d).

In vivo Degradation

Substrate	Tissue or Excreta	Products
γ-HCH	Urine	γ-HCH; PCP; 2,3,4,5-TeCP; TeCCOL free and glucuronide; 2,3,4,6/or 2,3,5,6-TeCP; PCB; 2,4,6-TCP; γ-PCCH; 1,2,3,4-TeCB; 1,2,3-TCB; 1,2,4-TCB; 2,3,5-/or 2,3,6-/or 2,4,5-/or 3,4,5-TCP.
	Feces	γ-HCH
	Blood	γ-HCH; PCP; 2,3,4,5-TeCP; 2,3,4,6-/or 2,3,5,6-TeCP; PCB; γ-PCCH; 2,3,5-/or 2,3,6-/or 2,4,5-/or 3,4,5-TCP.
	Liver	γ-PCCH; PCP; 2,3,4,6-/or 2,3,5,6-TeCP.
	Kidney	γ-HCH; γ-PCCH; PCB; 2,4,6-TCP; 1,3,5-TCB; 2,3,4,6-/or 2,3,5,6-TeCP.
PCB	Urine	PCB; PCP; 2,3,4,5-TeCP; 1,2,3,4-TeCB; 2,4,6-TCP; 1,2,3-TCB; 1,2,4-TCB; 2,3,4,6-/or 2,3,5,6-TeCP; 2,3,5-/or 2,3,6-/or 2,4,5-/or 3,4,5-TCP (1,3,5-TCB present in liver).
	Blood	PCB; PCP; 2,3,4,5-TeCP; 2,3,4,6-/or 2,3,5,6-TeCP; 2,3,5-/or 2,3,6-/or 2,4,5-/or 3,4,5-TCP.
γ-PCCH	Urine	γ-PCCH; PCP; 2,3,4,6-/or 2,3,5,6-TeCP; TeCCOL free and glucuronide; 2,4,6-TCP; 1,2,4,5-/or 1,2,3,5-TeCB; 2,3,5-/or 2,3,6-/or 2,4,5-/or 3,4,5-TCP; 2,3,4,5-TeCP; PCB; 1,2,3,4-TeCB; 1,2,3-TCB; 1,3,5-TCB.
	Feces	γ-PCCH; PCB; 2,4,6-TCB; 1,2,3-TCB; 1,3,5-TCB.
	Liver	TeCB or 1,3,5-TCB (partial analysis)
	Kidney	1,2,3-TCB; 1,2,4-TCB; 1,3,5-TCB, 1,2,4,5-/or 1,2,3,5-TeCB; 2,4,6-TCP; PCB.
	Blood	γ-PCCH; PCP

PCP	Urine	PCP; 2,3,4,5-TeCP; 2,3,4-TCP; 2,3,4,6-/or 2,3,5,6-TeCP. All were present both free and as glucuronides.

β-HCH, γ-HCH, δ-HCH, δ-PCCH, and 1,3,5-TCB were administered to rats. Hydroxylation and substitution of GSH for chlorine were the primary enzymatic mechanisms for HCH metabolism. Hydroxylation initiated production of 2,4,6-TCP. The second pathway leads to isomers of dichlorophenylmercapturic acid (Portig et al., 1975).

Weanling female Sprague-Dawley rats were fed 400 ppm lindane in the diet. Urine was collected and analyzed. MS and NMR were used to identify several metabolites as glucuronide and sulfate conjugates of 2,4,5,6-tetrachloro-2-cyclohexen-1-ol (2,4,5,6-TCCOL) and 2,3,4,6-tetrachloro-2-cyclohexen-1-ol (2,3,4,6-TCCOL). Incubation of lindane under N_2, with an NADPH generating system, produced a chlorinated neutral metabolite which was identified as γ-3,4,5,6-tetrachlorocyclohex-1-ene (Chadwick et al., 1978).

Lindane was administered in sunflower oil to rats. The livers were removed and then extracted. Gas chromatography indicated the presence of 1,2,4-TCB, γ-PCCH, pentachlorobenzene (PCB), and 2,3,4,6-TCP (Kujawa et al., 1974). When PCCH was used, 1,2,3,5- and/or 1,2,4,5-TeCB and 1,3,5-TCB were observed (Engst et al., 1978).

Male Wistar rats were i.p. administered lindane and urine was collected for 48 h. After adjustment to pH 3, the urine was extracted and then analyzed by GC-MS. In addition to S-2,4-dichlorophenylmercapturic acid (2,4-DCPMA), the 4-chloro-, 3,4-dichloro-, 2,5-dichloro-, 2,3,5-trichloro-, and 2,4,5-trichloro- phenylmercapturic acids were also identified. When pentachlorocyclohexene (PCCH) was administered, 2,4-DCPMA was almost the only mercapturic acid metabolite. Hexachlorocyclohexene was also administered i.p. to rats. Analyses of the metabolites indicated a strong resemblance to those of lindane. *In vitro* studies with rat liver supernatant (100,000xg) and GSH gave somewhat different results than *in vivo*. This is summarized in table I (Kurihara et al., 1977b).

In vitro studies also gave 4-CPG, almost entirely, from (35/46)-BTC and (346/5)BTC; 3-CPG from (34/5)-1,3,4,5-tetrachlorocyclohexene. Because of the low level of activity of lindane in this *in vitro* system, GSH conjugates were not detectable after 5 h at 37C (Kurihara et al., 1977b). In the presence of rat liver microsomes and NADPH, all isomers of BHC produced 2,4,6-trichlorophenol (2,4,6-TCP). The order of reactivity was δ>Σ>α>γ>β. In addition to 2,4,6-TCP, the following was observed:

Substrate	Product
γ-BHC	(36/45)-HCCH; (36/45)-PCCH
α-BHC	(346/5)-PCCH
δ-BHC	(35/46)-PCCH
β-BHC	(no PCCH or HCCH)

Additionally, 2,4,5-TCP and 2,3,4,6-tetrachlorophenol (TeCP) were obtained from five PCCH isomers and four HCCH isomers, respectively, as major metabolites. PCCH also yields one or two stereoisomers of pentachlorocyclohexenol.

Substrate	Product
(356/4)-PCCH	2,4,5-TCP (53%)
(346/5)-PCCH	2,4,5-TCP (6%); (345/6)-PCC-3-OL; (36/45)-PCC-3-OL
(346/5)-BTC	mainly (36/45)- and (345/6)-tetrachlorocyclohexen-3-ol

In an attempt to elucidate the mechanism involved in the formation of the phenols, it was found that chromic acid oxidation of (36/45)-4,5,6-trichlorocyclohexen-3-ol gave only 2,4-dichlorophenol (2,4-DCP) not 2,3-DCP. This is consonant with the finding that (356/4)-PCCH yields *in vitro* 2,4,5-TCP and not 2,3,5-TCP and HCCH isomers yield 2,3,4,6-TeCP. These studies indicated three pathways of formation of phenols from lindane:

1. Direct hydroxylation of lindane/derivatives and formation of *gem*-chlorohydrins. Subsequent decomposition to pentachlorocyclohexanones and dehydrochlorinations of tautomers give rise to 2,4,6-TCP.

2. Formation of HCCH and PCCH which give rise to *gem*-chlorohydrins through an ene-like reaction with activated oxygen. These products spontaneously form enones, tautomerize, and yield 2,4,5-TCP and 2,3,4,6-TeCP from PCCH and HCCH, respectively.

3. Direct hydroxylation of benzene analogs which form.

The requirement of this *in vitro* system for molecular oxygen and NADPH and its inhibition by CO suggested the participation of cytochrome P-450 in this reaction (Tanaka et al., 1977b).

Similar results and conclusions were reached in other *in vitro* studies with delta HCH and rat liver microsomes. This isomer was found to exhibit a greater rate of formation of 2,4,6-TCP than the other HCH isomers. When NADPH was omitted from the incubation mixture, no 2,4,6-TCP was observed. The presence of CO also inhibited formation of this phenol. At pH 7.4 and 37C in the presence of air and NADPH and incubation with α-, β-, δ- or Σ-HCH, the only chlorophenol produced was 2,4,6-TCP. In the presence of the γ-isomer, several phenols were formed, including

TABLE I

Substrate	In vivo								In vitro									
	CPMA		DCPMA				TCPMA		DCPG						TCPG			
	3-	4-	2,3-	2,4-	2,5-	3,4-	2,3,5-	2,4,5-	2,3-	2,4-	2,5-	2,6-	3,4-	3,5-	2,3,4-	2,3,5-	2,3,6-/or 3,4,5-	2,4,6-
Lindane	tr	++	+	++	+	++	++	++										
HCCHE (36/45)	tr	+	+	++	+	+	++	++									+	+
(35/46)															+		+	
(346/5)															+	+	+	
PCCHE (36/45)	0	tr	0	+++++	+	0	tr	tr	0	+++++	0	+	+	0				
(35/46)									0	++++	0	0	++	0				
(34/56)									0	++	+++	+	+	0				
(356/4)									0	+++	+	++	++	0				
(346/5)	0	+++	0	+	++	++	tr	tr	0	+	+	0	++++	0				

CPMA = S-chlorophenylmercapturic acid
TCPMA = S-trichlorophenylmercapturic acid
CPG = S-chlorophenylglutathione
DCPG = S-dichlorophenylglutathione
TCPG = S-trichlorophenylglutathione

(Kurihara et al., 1977)

2,4,6-TCP and 2,3,4,6-tetrachlorophenol (2,3,4,6-TeCP). *In vitro* studies also showed that 1,3,5-TCB produced 2,4,6-TCP but 1,2,3-TCB produced none. In the case of γ-HCH, δ-PCCH, γ-PCCH, and 1,2,4-TCB, although 2,4,6-TCP was found, it was not the sole chlorophenol (Stein et al., 1977).

Major phenolic metabolites of PCCH isomers and 1,2,4-TCB were 2,4,5- and 2,3,5-TCP. The major phenolic metabolite of α-, β-, γ-, and δ-HCH was 2,4,6-TCP. Only a small amount of 2,3,4,6-TeCP was produced *in vivo* from γ-PCCH. Rat liver microsomes converted α-, β-, γ-, and δ-HCH to TCP when NADPH and O_2 were added. This system formed 2,3,4,6-TeCP and 2,4,6-TCP from γ-HCH. γ- and δ-PCCH were converted primarily to 2,4,5/2,3,5-TCP (Stein and Portig, 1976).

	In vitro
Substrate	Product
δ-HCH	2,4,6-TCP
γ-HCH	2,4,6-TCP; 2,3,6-TCP; 2,4,5-/or 2,3,5-TCP; 2,3,4-TCP; 2,3,4,6-TeCP
δ-PCCH	2,4,6-TCP; 2,4,5-/or 2,3,5-TCP; 2,3,4-TCP; 2,3,6-TCP
γ-PCCH	2,4,6-TCP; 2,4,5-/or 2,3,5-TCP
1,2,3-TCB	2,3,4-TCP; 2,3,6-TCP
1,2,4-TCB	2,4,6-TCP; 2,3,4-TCP; 2,3,6-TCP; 2,4,5-/or 2,3,5-TCP
1,3,5-TCB	2,4,6-TCP

(Stein et al., 1977)

Under an atmosphere of nitrogen and in the presence of rat hepatic microsomes plus NADPH, lindane degraded to give (346/5)-TeCH. (36/45)-HCCH gave mostly 1,2,4-TCB. Some *o*-DCB was also observed. GC-MS was used to identify the metabolites (Kurihara et al., 1978).

After i.p. injection of 1,2,3-trichlorobenzene (1,2,3-TCB) into rats, no 2,4,6-TCP was observed; 1,2,4-TCB produced about 1% 2,4,6-TCP; 1,3,5-TCB produced large amounts of 2,4,6-TCP. In addition, it was found that 1,2,4-TCB yielded 2,4,5- and 2,3,5-TCP; 1,2,3-TCB yielded 2,3,4-TCP and 3,4,5-TCP; and corresponding positional isomers of trichlorothiophenol. The latter was not observed after 1,3,5-TCB application. However, a a hydroxydichlorothiophenol was observed. Both isomers of PCCH yield 2,4,6-TCP but in amounts less than 1%. The major phenols from PCCH were 2,4,5- and/or 2,3,5-TCP. Some dichlorothiophenols including the 2,4-isomer were also present (Stein et al., 1977).

Accumulation ratios for eggs were calculated when HCH was fed to laying hens for 16 weeks.

Compound	Accumulation Factor Egg	Accumulation Factor Fat
α-HCH	2	2
β-HCH	13	15
γ-HCH	2	2

Depletion $t_{1\ 2}$ = 1.5 to 2 weeks for α- and γ-HCH and 6 to 8 weeks for β-HCH (Kan and Rooyen, 1978).

Laying hen pheasants were administered lindane-^{14}C in gelatin capsules and with seed treated with labeled lindane. Residues were determined in eggs and in tissues of hatched chicks. Residues in eggs from birds given treated seed showed a greater variation in total ^{14}C than from capsule-fed birds. Egg yolks were analyzed by ECGC on three columns and by use of Coulson conductivity detector on two columns. Confirmation was by GC/MS. Chick tissue contained: 1,2-DCB; 1,2,4-TCB; 1,2,3,4-TeCB; 1,2,3,5-/or 1,2,4,5-TeCB; γ-PCCH; PCB. Yolks contained these metabolites plus 1,3,5-TCB and 1,2,3-TCB (Saha and Burrage, 1976).

A glutathion-dependent enzyme, obtained from the soluble fraction of chicken liver homogenates, metabolized lindane *in vitro* anaerobically. In addition to γ-HCH, the α- and δ-isomers were metabolized but the β-isomer was not. Metabolism of lindane in this system was rapid with 98% metabolized in 5 h. About 66% of the metabolites were soluble in petroleum. Metabolites were identified by MS and GC: *o*-dichlorobenzene; *m*-dichlorobenzene; *p*-dichlorobenzene; 1,2,3-TCB; 1,2,4-TCB; γ-PCCH; 2,3-DCP; 2,4-DCP; 2,4,6-TCP; chlorobenzene; trichlorocyclohexene (2 isomers); dichlorocyclohexadientriol; chlorophenol; trichlorocyclohexenol; and trichlorocyclohexandiol. A number of conjugated metabolites were also present but were not identified (Foster and Saha, 1978).

Rats were pretreated with seven organochlorine pesticides and their effects on enzyme induction and lindane metabolism was compared. Relative effects are summarized (Table II) (Chadwick et al., 1977).

Animals in these tests were exposed to lindane for 96 h in flowing sea water. Bioconcentration factors are lindane concentrations in whole-body tissues of surviving animals (Schimmel et al., 1977).

TABLE II

Compound fed	Total ^{14}C Excreted	^{14}C in Urine	Metabolite Excretion in Urine											
			Chlorophenol				Neutral extract	% PCCOL in		% of total chlorophenol				
			Neutral	Free	Conj.	Polar		Total free Cl-phenols	Total conj. Cl-phenols	2,4,6-TCP	2,3,5-TCP	2,4,5-TCP	2,3,4,6-TeCP	2,3,4,5-TeCP
Chlordane	+++++	+++++	++	++	++++	++++	+++	++	++++	++++	++++	+++	+++	+
DDT	++++++	++++++	++++	+++	+++	+++	++++	++++	++	++	++	+++	+++	++++++
HCB	+++	+++	+++	+++	+++	+++	+++++	++++	+++	+++	+++	++++	+++	++
Mirex	+++++	+++++	++	++	+++	++++	+++	+++	++++	++++	+++++	++	+++	+
Penphene	+	+	++	++	++	+++++	++	++++	+++	++++	++++	+++	++	++++
Pentac	++	++	++++	++	+++	++++	++++	++++	+++	++++	++++	++++	+++	++
Toxaphene	+++	+++	++++	+++	+++	++++	++++	+++	+++	+++	+++	+++	+++	++
Control	++	+	++++	++	++	++++	+++	++++	++	+++++	+++	++++	++	++++

(Chadwick et al., 1977)

TABLE III

Lindane bioconcentration in estuarine animals

Test species	Water conc. (μg/L)	Bioconc. factor
Pink shrimp (*Pinaeus duorarum*)	0.033	(N.D.)
	0.073	(N.D.)
	0.13	77
	0.23	143
	0.62	32
Pinfish (*Lagodon rhombiodes*)	18.4	201
	23.0	287
	31.3	167
Grass shrimp (*Palaemonetes pugio*)	1.0	80
	1.6	68
	3.1	27
	5.5	25
Sheepshead minnow (*Cyprinodon variegatus*)	41.9	477
	50.3	417
	86.1	337
	108.7	727

When exposed to α-HCH, the accumulation factor in crustacean (*Artemia salina*) was 60-90 and 500 in *Lebistes reticulatus*. The $t_{1/2}$ = 48-72 h in *Artemia* and less than 10 h in *Lebistes* (Canton et al., 1978).

HCB was identified as a plant metabolite of lindane. Identification of this product by GC and MS followed Al_2O_3 separation (Steinwandter, 1976a). When α-HCH was applied to plants, the level of β-HCH on the plants was shown to increase, showing transformation of α-HCH to β-HCH (Steinwandter, 1978). Studies with γ-HCH showed that HCB, α-HCH and β-HCH can be formed from lindane on plants (Steinwandter and Schluter, 1978).

Lindane was applied to beans (*Phaseolus vulgaris*) and maize (*Zea mays*). Analyses of bean plants indicated the presence of γ-PCCH and 1,2,4-TCB. In addition to these two compounds, 1,2,3-TCB was observed in maize extracts (Mostafa et al., 1974). When maize plants were exposed to γ-PCCH in aqueous solution, metabolites observed with GC and MS were *m*-DCB; 1,2,4-TCB; 1,2,4,5-TeCB; 1,2,3,4-TeCB; 2,4,5-TCP; and 2,3,5-TCP. When plants were used, in addition to *m*-DCB, 1,2,4,5-TeCB, and 2,4,5-TCP, compounds identified as 1,2,3-TCB and 2,4,6-TCP were observed (Moza et al., 1974).

γ-HCH was added to culture solutions of the unicellular algae Chlorella vulgaris Beijerinck and Chlamydomonas reinhardtii Dangeard in axenic culture. Chromatographic analyses indicated the formation of a compound identified as PCCH (Sweeney, 1969).

In mold culture containing lindane, γ-PCCH and PCB/or HCB were observed (Kujawa et al., 1976). In other studies with mold cultures, lindane metabolites were identified by use of 5 different GC columns and mass spectrometry. Sixteen compounds were observed: 1,2-DCB; 1,4-DCB; 1,2,3-TCB; 1,2,4-TCB; 1,3,5-TCB; 2,3,4-TCP; 2,4,6-TCP; 1,2,3,4-TeCB; 1,2,4,5-/or 1,2,3,5-TeCB; 2,3,4,5-TeCP; 2,3,4,6-/or 2,3,5,6-TeCP; γ-PCCH; PCB; PCP; HCB; and TeCCOL. There were also at least four unidentified metabolites, one of which is believed to be 2,3,4,5,6-pentachlorocyclohexen-2-ol-1 (PCCOL). The degradation of γ-PCCH produced large amounts of TeCCOL and PCP. 2,3,6-TCP was also observed. PCP degradation gave 2,3,4,5-TeCP mainly plus small amounts of 2,3,4,6-/or 2,3,5,6-TeCP. In a 52-day test time, there was no indication of degradation of 1,2,4,5-TeCB when added to a mold culture. Addition of 1,2,3,5-TeCB to a culture produced 2,3,4-TeCP; 1,2,3,4-TeCB produced mainly 2,3,4,5-TeCP. Some 1,2,3-TCB and unidentified metabolites were also observed (Engst et al., 1977).

In vitro studies with fly homogenates showed that deuteriated lindane breakdown was six-fold slower than non-deuteriated lindane. Lindane-treated houseflies produced (36/45)-1,2,3,4,5,6-hexachlorocyclohexene (HCCH), (36/45)-PCCH, PCB, and tri- and tetrachlorobenzenes. PCB was identified as an in vivo metabolite of (36/45)-HCCH but not from the (36/45)-, (35/46)-, (34/56)-, (346/5)-, and (356/4)-isomers of PCCH. In the presence of the housefly microsomal fraction and NADPH, lindane metabolism produced (36/45)-HCCH, (36/45)-PCCH, and (346/5)-PCCH. The latter was not observed in the in vivo studies. With the post-microsomal fraction and glutathione, (346/5)-PCCH breakdown was much more rapid than that of (36/45)-HCCH or (36/45)-PCCH. Other in vitro observations showed no PCB from lindane but a small amount from (36/45)-HCCH. Formation of S-(2,4-dichlorophenyl)glutathione indicated conjugation probably occurred at position 6 of (36/45)-PCCH since conjugation at position 3 would not give this glutathione conjugate. A similar mechanism would occur with (346/5)-PCCH or (36/45)-HCCH. From this it appears that a cis-dehydrogenation and a cis-dehydrochlorination leads to (36/45)-HCCH and (346/5)-PCCH, respectively, and that a trans-dehydrochlorination leads to (36/45-PCCH. PCB was derived from (36/45)-HCCH. Thus, glutathione conjugation is believed to occur at the PCCH or HCCH stage (Tanaka et al., 1976a and b).

Seventy-one microorganisms isolated from a loamy sand soil exhibited good growth on γ-HCH and produced chloride in the medium. Thirteen of these organisms were further studied and shown to degrade lindane to varying degrees. Pseudomonas sp. No. 62 produced PCB, γ-PCCH, α-TCCH, β-TCCH, and γ-TCCH. One other compound appeared to be 1,2,3,4-TeCB. Micromonospora sp. No. 1040 did not produce PCB and α-TCCH (Tu, 1976).

Cell-free *Clostridium sphenoides* preparations were used to study lindane degradation. The activity was glutathione dependent and appeared to associate with membrane fraction. Lindane (γ-HCH) was metabolized to γ-isomer of 3,4,5,6-tetrachlorocyclohex-1-ene (γ-TCCH) (Heritage and MacRae, 1977a). Additional studies with *Clostridium sphenoides* showed that the α- and γ-HCH isomers were degraded to δ- and γ-TCCH, respectively (Heritage and MacRae, 1977b).

Of 354 microorganisms isolated from the environment, 71 were capable of metabolizing γ-HCH. Using *Pseudomonas putida*, it was shown that there were two patterns of metabolism of γ-HCH and that in measure they were related to the nutritional properties of the medium. On standard yeast-mannitol media, *P. putida* metabolized γ-HCH primarily to γ-PCCH. Small amounts of γ-BTC, α-HCH and CO_2 were also formed. The pattern of γ-HCH metabolism was changed by the addition of additives to the media. Addition of NAD produced the most notable change with the γ-BTC jumping from 0.5 to 19%. At the same time, γ-PCCH dropped from 7 to 2%. These studies also indicated that the first step of γ-HCH metabolism was oxidative and required NAD; that the second step was stimulated by FAD. The NAD requiring route produced γ-BTC and α-HCH whereas the other route was one of non-specific metabolism of γ-HCH to γ-PCCH (Matsumura et al., 1976).

Under anaerobic conditions, *Clostridium butyricum*, *C. pasteuranum* and *Citrobacter freundii* rapidly degraded γ-HCH. Several bacteria belonging to the Bacillaceae and Enterobacteriaceae also degraded γ-HCH but only weakly. Analyses indicated the presence of α- and β-HCH, several TeCBs and/or TCBs. The compound identified as γ-TCCH, was also formed by all species that anaerobically degraded γ-HCH. No PCCH was observed. Rate of dechlorination of HCH isomers was $\gamma>\alpha>\beta\geq\delta$ (Jagnow et al., 1977). *Clostridium rectum*, isolated from paddy field soil, degraded γ-HCH rapidly. γ-TCCH was identified as the dominant intermediate in the degradation (Ohisa and Yamaguchi, 1978a). Other anaerobic bacteria isolated from soil-peptone cultures, capable of decomposing BHC, were identified as species of *Clostridium* also (Ohisa and Yamaguchi, 1978b).

Soils were treated with lindane-^{14}C. The pattern of metabolites observed is summarized.

Metabolite	Soil			
	Organic		Mineral	
	Moist	Submerged	Moist	Submerged
DCB (*m*/or *p*)	++++	+++	+	+
1,2,4-TCB	+	+	N.D.	++
1,3,5-TCB	++	+	N.D.	++

Residues of HCH in various commodities included PCCH. α- and δ-PCCH were found in milk samples. γ-PCCH was found in dehydrated vegetables and in wool fat but not in milk (Stijve and Cardinale, 1972).

When rats were pretreated with γ-HCH, DDT, or DDT plus γ-HCH, the metabolism of γ-HCH was increased. Quantitative and qualitative differences in γ-HCH metabolism were observed. With γ-HCH-pretreatment, rats had higher glucuronyl transferase activity, greater GSH-dependent γ-HCH degradation, and lower level of MFO than DDT treated rats (Chadwick et al., 1971).

When placed in a model ecosystem, lindane gave rise to PCCH and about six unidentified compounds. PCCH accumulated only in the snail Physa. Lindane accumulated in the snail and the fish Gambusia. The calculated ecological magnification factor was found to be 456 and 560, respectively (Metcalf et al., 1973b).

Lindane (γ-HCH) was dissolved in petroleum ether, acetone or water and exposed in quartz cuvettes to UV light with emission beginning at 230 nm. Analyses of these exposed materials indicated that there was some isomerization of γ-HCH to α-HCH and δ-HCH. PCB and PCCH also formed. In the aqueous solution, hydroxylation and polymerization probably also occurred (Steinwandter, 1976c). When heated in dimethyl sulfoxide, (35/46)-HCCH isomerized to (346/5)-HCCH. This in turn isomerized partially to (34/56)-HCCH (Kurihara et al., 1976).

Electrochemistry indicated that, under anaerobic conditions, γ-BTC should form from lindane and that this should lead to benzene formation. Incubation of lindane in sewage sludge showed that γ-BTC was an intermediate and that benzene was the final reduction product (Beland et al., 1976).

Ni_2B-$NaBH_4$ reduction of lindane was carried out in methanol, ethanol or 2-propanol. Benzene, cyclohexene and cyclohexane were formed in addition to chloride (Dennis and Cooper, 1977).

Chlorobenzenes were administered i.p. in oil to rabbits. Urine and feces were analyzed. The results are summarized in the following table.

Compound Administered	Products
1,2,4-TCB	2,4,5-TCP; 2,3,5-TCP
1,2,3-TCB	2,3,4-TCP; 2,3,6-TCP; 3,4,5-TCP
1,3,5-TCB	2,3,5-TCP; 2,4,6-TCP; unidentified compound believed to be a dichlorobenzene with 2 hydroxyl and one methoxyl group.

1,2,3,4-TeCB	2,3,4,5-TeCP; 2,3,4,6-TeCP
1,2,3,5-TeCB	2,3,4,5-TeCP; 2,3,4,6-TeCP; 2,3,5,6-TeCP
1,2,4,5-TeCB	2,3,5,6-TeCP
PCB	2,3,4,5-TeCP; PCP

(Kohli et al., 1976a)

Studies with cytochrome P-450 showed that all three TCB isomers interact with this hemoprotein. The affinity of these compounds with cytochrome P-450 was in the order 1,2,3- > 1,2,4- > 1,3,5-TCB (Egyankor and Franklin, 1977).

In cyclohexane and 2-propanol, photochemical dechlorination of 1,2,4-TCB produced primarily 1,3- and 1,4-DCB (Akermark et al., 1976).

Biodegradability of lindane analogs was investigated in vivo and in vitro. Exposure of houseflies to lindane analogs indicated that penetration and metabolism does not follow simple first-order kinetics. The order of degradation susceptibility was 1-SMe∿3-SMe>1-OEt∿1-OMe∿3-OEt> 3-OMe>1,2-H,OMe>1-Me>lindane (Kurihara et al., 1977a).

Substrate	Metabolite
1-SMe	$1\text{-}\overset{\overset{O}{\|}}{S}\text{Me}$
3-SMe	$3\text{-}\overset{\overset{O}{\|}}{S}\text{Me}$
1-OEt	1-OH
3-OEt	3-OH
1-OMe	1-OH; unidentified dechlorinated compound
3-OMe	3-OH
1,2-H,OMe	1,2-H,OH
1-Me	$1\text{-CH}_2\text{OH}$

(Kiso et al., 1977; Kurihara et al., 1977a; Nakajima et al., 1974)

In the case of 1-S-CH_3, GC-MS also showed the presence of (356/4)-PCCH (Kiso et al., 1977; Nakajima et al., 1974).

The three tetrachlorophenols were administered intraperitoneally to rats. Urine was collected and analyzed. When 2,3,4,5- and 2,3,4,6-tetrachlorophenol were used, trichloro-*p*-hydroquinone was found in urine in small amounts. Most of these materials was excreted unchanged. With 2,3,5,6-tetrachlorophenol, about 35% of the dose was excreted in urine as the tetrachloro-*p*-hydroquinone (Ahlborg and Larsson, 1978).

BIFENOX (Mowdown, MC-4379, Methyl 5-(2,4-dichlorophenoxy)-2-nitrobenzoate) [2,4-Dichlorophenyl 3'-carbomethoxy-4'-nitrophenyl ether]

When applied as a preemergent to greenhouse soil, bifenox exhibited a half-life of 3 to 7 days. Over a 313-day sampling period, the metabolites recovered and identified included: 5-(2,4-dichlorophenoxy)-2-nitrobenzoic acid (II); 2,4-dichlorophenyl 4-nitrophenyl ether (IV) (nitrofen); and 5-(2,4-dichlorophenoxy)anthranilic acid (III). The predominant metabolite found in Frederick clay loam soil was identified as compound II. When tested *in vitro* with shoot-tissue macerates, bifenox was not degraded by corn (*Zea mays* L.) or soybeans [*Glycine max* (L.) Merr.] and to only a slight extent by velvetleaf (*Abutilon theophresti* Medic.). Some unidentified materials, believed to be conjugated, were also produced in the soil (Leather, 1976; Leather and Foy, 1977).

Bifenox degradation was studied under flooded and upland moisture conditions in the laboratory. Nitrophenyl-^{14}C-ring-labeled bifenox, three arable soils from paddy fields, and a subsoil from forest were used. Differences in the degradation pattern between soils were small; difference between flooded and upland conditions were large. In flooded paddy soil, $t_{1/2}$ = 4 d; in nonflooded paddy soil, $t_{1/2} \approx$ 6 d. Under flooded soil conditions, nine products, six minor and three major, were detected. Eight were identified. The major compounds were identified as

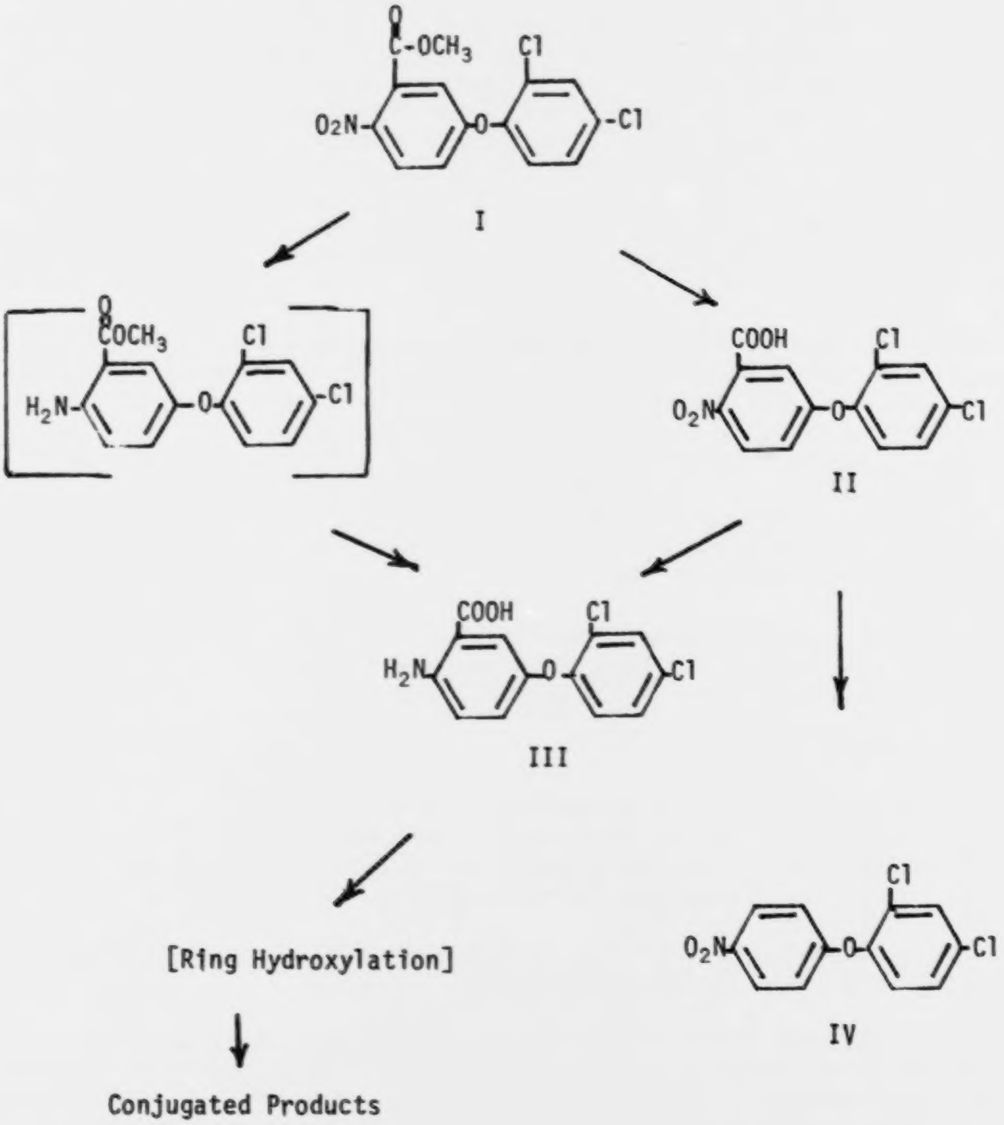
II. 5-(2,4-dichlorophenoxy)-2-nitrobenzoic acid,
III. methyl 5-(2,4-dichlorophenoxy)anthranilate, and
IV. 5-(2,4-dichlorophenoxy)anthranilic acid;

and the minor compounds

V. 5-(2,4-dichlorophenoxy)salicylic acid
VI. methyl 5-(2,4-dichlorophenoxy)-2-acetamidobenzoate,
VII. methyl 5-(2,4-dichlorophenoxy)-2-formamidobenzoate, and
VIII. 5-(2,4-dichlorophenoxy)-2-acetoamidobenzoic acid.

Another compound was identified as 5-(2,4-dichlorophenoxy)-2-formamidobenzoic acid (IX) (Ohyama and Kuwatsuka, 1978b).

Bifenox was added to a rice paddy model ecosystem. Analyses indicated that tissue storage was minimal. Hydrolysis readily occurred to produce 2,4-dichlorophenyl 3'-carboxy-4'-nitrophenyl ether and the amine analog of bifenox. Conjugation of these compounds apparently occurred in daphnia, mosquito and fish. The acetate was observed. The snail was unable to hydrolyze the bifenox. In this system, the EM (ecological magnification) value for bifenox in fish was calculated to be approximately 50 (Lee et al., 1976).


I
II
III
IV
[Ring Hydroxylation]
Conjugated Products

Biphenyl

Studies with biphenyl indicated that albino rats handled biphenyl by a mechanism which involved sulfur of sulfur containing amino acids (West, 1940). Rats fed biphenyl, excreted a compound identified as *p*,*p*'-dihydroxybiphenyl. Another compound was also obtained that is believed to be diphenylmercapturic acid (West et al., 1953). In other studies, 3,4-dihydroxybiphenyl and *p*-β-D-glucuronisidobiphenyl were isolated and identified (West et al., 1955). Both 4-hydroxy- and 4,4'-dihydroxybiphenyl are excreted by rats to a great extent in the bile as glucuronides (Millburn et al., 1967). In rat livers from untreated rats, the 4-hydroxybiphenyl formed the sulfate conjugate preferentially. However, after induction, glucuronide formation was as prominent as sulfate formation or even exceeded sulfation. With 2-hydroxybiphenyl only the glucuronide was observed (Kahl et al., 1978).

^{14}C-Biphenyl was orally administered to rats and urine was collected. After 96 h 92% of the radioactivity had been excreted. Urinary excretion accounted for more than 84% of the administered label (75.8% within 24 h) and fecal excretion for 7.3% (5.8% within 24 h) of the radioactivity. Trace amounts of $^{14}CO_2$ were also observed in expired air. Nearly 30% of the dose was present as conjugated phenols (Meyer et al., 1976a). Metabolites were identified by mass spectroscopy and quantified by gas chromatography after conversion to trimethylsilyl derivatives. The major metabolites were identified as 4-hydroxy- (7.7%) and 4,4'-dihydroxybiphenyl (11.4%). Within 24 h, 5.2% of the dose appeared in the bile as conjugates of 4-hydroxy-, 4,4'-dihydroxy-, and 3,4,4'-trihydroxybiphenyl. Other metabolites also detected included 3,4'-dihydroxybiphenyl, 3,4'-dihydroxy-4-methoxybiphenyl, and 4,4'-dihydroxy-3-methoxybiphenyl.

	Rat			Pig		
Biphenyl metabolites	Urine	Feces	Bile	Urine	Feces	Bile
2-hydroxy-	+	+	+	+	-	-
3-hydroxy-	+	+	+	+	-	-
4-hydroxy-	+	+	+	+	-	-
2,5-dihydroxy-	+	-	-	-	-	-
3,4-dihydroxy-	+	-	+	+	-	-
3,4'-dihydroxy-	+	-	+	+	-	-
4,4'-dihydroxy-	+	+	+	+	-	-
3,4,4'-trihydroxy-	+	+	+	+	-	-
3-hydroxy-4-methoxy-	+	-	+	+	-	-
4-hydroxy-3-methoxy-	+	-	+	+	-	-
3,4'-dihydroxy-4-methoxy-	+	-	+	+	-	-
4,4'-dihydroxy-3-methoxy-	+	-	+	+	-	-

Analyses of urine indicated the presence of only trace amounts of free phenolic biphenyl metabolites. While urine metabolites were present mainly as conjugates, fecal metabolites were unconjugated. Biliary metabolites were also present in conjugated form (Meyer and Scheline, 1976; Meyer et al., 1976a).

After female pigs were administered biphenyl in soya oil, no free phenolic metabolites were observed in the urine. No phenolic metabolites of biphenyl were detected in feces or bile. In 4 days, 27.6% of the dose appeared in the urine. Of this, about 19% was in the form of the 4-hydroxy analog; 2.7% as the 2-hydroxy; and 2.0% as the 4,4'-dihydroxy analog. When biphenyl was administered in propylene glycol, the four day urinary excretion rose to 44.8% of the dose and 32% of this appeared as 4-hydroxybiphenyl. The 2-hydroxy and 4-hydroxy derivatives accounted for 4.3 and 2.8%, respectively (Meyer et al., 1976b).

When biphenyl was administered to guinea pigs, 32.9% of the dose was excreted in the urine. Of this, about 1.8% was present in the form of free phenols as the 3- and 4-monohydroxy metabolites. Analyses of the conjugated metabolites showed that the major metabolite was the 4-hydroxy derivative. Analyses of feces showed only the presence of 3-hydroxy- and 4-hydroxybiphenyl. The 4,4'-dihydroxy analog as well as the 3- and 4-monohydroxybiphenyl derivatives were detected in bile (Meyer, 1977).

Rabbits, administered biphenyl, excreted less than 1% of the dose in a free form in the urine. The total amount of phenolic biphenyl metabolites was 49.1% after 4 days. About 35% of this was the 4-hydroxybiphenyl. Feces and bile contained small amounts of the 4-hydroxybiphenyl only (Meyer, 1977). After i.v. injection of biphenyl into rabbits, 4-hydroxy, 4,4'-dihydroxy-, and 2-hydroxybiphenyl were identified as metabolites in the urine. After injection of 4-hydroxybiphenyl, a metabolite was observed that indicated cleavage of a benzene nucleus (Berninger et al., 1968).

The *in vitro* metabolism of biphenyl by tissues of marine organisms was studied. 4-Hydroxybiphenyl and some 2-hydroxybiphenyl were produced by tissues of *Raja ocellata*, *Salvelinus fontinalis*, *Homarus americanus*, *Gerydon quinquidens*, *Cancer irroratus*, *Mytilus edulis*, *Asterias vulgaris*, and by zooplankton (Willis and Addison, 1974). Three marine organisms in aquaria were exposed to biphenyl. 2-Hydroxybiphenyl was the most prominent metabolite in all cases. Results are summarized in the following table (Meyer and Bakke, 1977).

	2-OH		4-OH		4,4 -(OH)$_2$	
	Water	Tissue	Water	Tissue	Water	Tissue
Cirolana borealis Liljeborg	+	+	+	-	+	-
Buccinum undatum L.	+	+	+	-	tr	tr
Ophiocomina nigra Abildgaard	+	+	+	+	-	+

Biphenyl hydroxylation was observed with rat hepatic preparations (Gerayesh-Nejad et al., 1975). Hepatocytes were isolated by enzymatic digestion of liver slices. After washing and re-suspension, these hepatocytes were incubated with labeled biphenyl. Analyses of the incubation mixtures indicated that the primary metabolite was 4-hydroxybiphenyl, largely present as glucuronide and sulfate conjugates. Some 4,4'-dihydroxybiphenyl was present in conjugated form and some free 2-hydroxybiphenyl was also probably present. When the 2-hydroxy analog was incubated with hepatocytes, a conjugate formed. The 2,2'-dihydroxy analog was not detected free or conjugated (Wiebkin et al., 1976). In other studies, untreated rat hepatocytes metabolized biphenyl via hydroxylation at the 4-position. The glucuronide formed but the sulfate was the major metabolite. The 2- and 3-hydroxybiphenyls were also formed to a small extent. After induction, the 4-hydroxybiphenyl glucuronide was the dominant metabolite (Wiebkin et al., 1978).

Brewer's yeast, *Saccharomyces cerevisiae*, hydroxylated biphenyl exclusively to the 4-hydroxy derivative. A microsomal fraction was also prepared from yeast cells at 105000g. This too hydroxylated biphenyl to the 4-hydroxy analog. Loss of biphenyl hydroxylase activity agreed with loss of cytochrome P-450 when heated (Wiseman et al., 1975).

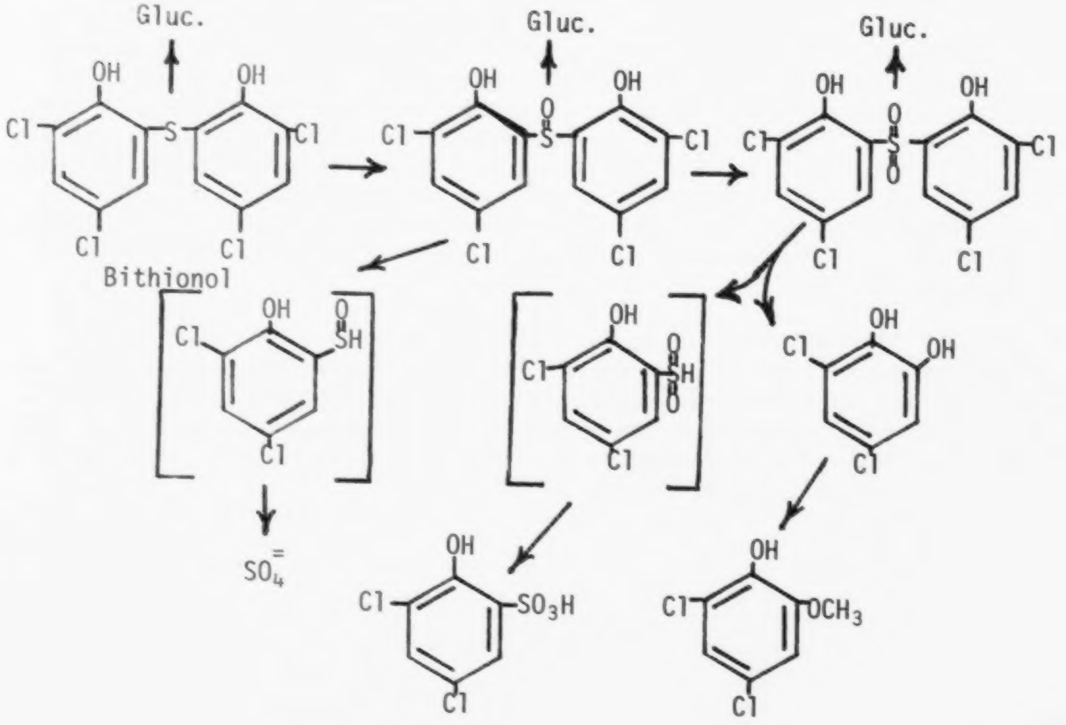
Microsomal preparations were obtained from mesocarp of avocado pear (*Persea americana*) and Syrian hamster hepatic tissue. Both 3,4-benzopyrene and safrole enhanced the microsomal 2-hydroxylase activity. However, enhancement of the plant system was significantly lower than that observed with the hamster hepatic microsomes. This was ascribed to the low benzopyrene hydroxylase activity in the avocado pear and the probability that an active metabolite is required for a carcinogen to enhance biphenyl 2-hydroxylase activity (McPherson et al., 1975).

Liver microsomes from male Long-Evans rats metabolized biphenyl only to the 4-hydroxy derivative. Pretreatment of rats with phenobarbital or 3-methylcholanthrene (3MC) significantly increased 4-hydroxylation and promoted 2-hydroxylation activity (Burke and Mayer, 1975). In other studies with hamster liver microsomes, phenobarbital and 3MC were used for microsome induction. The major metabolite, 4-hydroxybiphenyl, plus the 2-hydroxy analog, accounted for about 83% of the total biphenyl metabolites. Some 2,2'- and 4,4'-dihydroxy derivatives were also detected. Phenobarbital induced primarily 4-hydroxylation whereas 3MC induced both 2- and 4-hydroxylation about equally. This was apparently the result of affecting production and metabolism of the 2- and 4-hydroxy derivatives. NADPH-NADH specificities and pH optima were different for the 2- and 4-hydroxylations (Burke and Bridges, 1975).

BITHIONOL SULFOXIDE (Bitin-S) [Bis(3,5-dichloro-2-hydroxyphenyl) sulfoxide]

When ^{35}S-bithionol sulfoxide was orally administered to rats, urine, feces and bile were collected. Eight metabolites were observed in the urine. Paper chromatography and chemical tests identified one of these as inorganic sulfate. A strong acid was identified as 3,5-dichloro-2-hydroxysulfonic acid. Two other compounds were identified as bithionol sulfone and bithionol. In addition to these, three compounds were identified as glucuronides of bithionol, bithionol sulfoxide, and bithionol sulfone. One other metabolite was not identified. Except for free bithionol sulfone, the same metabolites were found in the bile as were present in urine. Quantitative differences, however, were large. The glucuronide of bithionol sulfone comprised 71% of ^{35}S in bile but only 16.5% in urine (Meshi et al., 1970).

When ^{35}S-bithionol, ^{35}S-bithionol sulfoxide, or ^{35}S-bithionol sulfone were fed to rats, urinary excretion of the metabolites indicated above was very low. Bithionol sulfoxide was excreted mainly in the feces. More than 90% of biliary radioactivity was in the form of glucuronides of the three compounds with more than 70% of the glucuronides present as bithionol glucuronide. The sulfone was metabolized to catechol and guaiacol (Meshi et al., 1970).



BOTRAN (DCNA) [2,6-Dichloro-4-nitroaniline]

After administration of DCNA to rats, 3,5-dichloro-4-aminophenol (DCAP) and 2,6-dichloro-*p*-phenylenediamine (DCPP) appeared in the urine. DCAP was given to female rats and analysis of collected urine showed that the DCAP was converted to DCPD and another unidentified compound, possibly the *N* -acetyl analog of DCPD (Gallo et al., 1976).

When urine of rats dosed with 2,6-dichloro-4-nitroaniline was hydrolyzed with acid, TLC showed two compounds. About 70% of the metabolites was accounted for by 4-amino-3,5-dichlorophenol. A small amount of 4-amino-2,6-dichloroaniline was also found. Feeding of the latter to rats did not give the 4-amino-3,5-dichlorophenol. Similar results were obtained *in vitro*. The same type metabolites were obtained with 2,6-dibromo-4-nitroaniline (Mate et al., 1967).

When soybean plants were exposed to DCNA in nutrient solution, the absorbed DCNA was found in shoots and roots. Analyses showed the presence of *N*-(4-amino-3,5-dichlorophenyl)malonamic acid. Callus tissue from shoot tips also produced this compound from DCNA (Kadunce et al., 1974).

Many fungi and bacteria tested were found capable of metabolizing DCNA to at least six metabolites. Two compounds were identified as 2,6-dichloro-*p*-phenylenediamine (DCPD) and 4-amino-3,5-dichloroacetanilide (ADCAA) by MS, NMR, and IR. *Pseudomonas cepacia* metabolized DCNA to ADCAA as the major metabolite. Most fungi formed only small amounts of these materials and formed DCNA metabolites different from those found in bacterial cultures. Low aeration favored conversion to DCPD and ADCAA by bacteria. In soil amended with glucose, ^{14}C-DCNA did not yield $^{14}CO_2$. ADCAA, DCPD and an azine isomer, from oxidative dimerization of DCPD, were observed. The azine is also formed by the action of horseradish peroxidase on DCPD (Van Alfen, 1973). In other studies, an unidentified pink colored compound was isolated from DCNA-treated soil (Wang, 1972).

In soil flooded and amended with glucose, recovery of added DCNA decreased to 3% after nine days. The major extractable metabolite was identified as 4-amino-3,5-dichloroacetanilide (ADCAA). DCPD and a compound that appeared to be a dimer of DCPD were also isolated. This latter compound also formed by the action of horseradish peroxidase on DCPD (Van Alfen and Kosuge, 1976).

BNOA [β-Naphthoxyacetic acid]

When applied to strawberry plants, no β-naphthol was detected. Levels of BNOA dissipated on the berries to <0.05 ppm in 5 to 6 days when sprayed once at 50 or 100 ppm. Leaves had 0.16 ppm and 0.25 ppm BNOA after 15 days when sprayed once at 50 or 100 ppm, respectively (Archer and Stokes, 1978).

BOMYL [O,O-Dimethyl O-2-(1,3-dicarbomethoxyprop-1-enyl)phosphate]

Cis- and *trans*-bomyl were degraded by mouse liver homogenates at about the same rate. The presence or absence of glutathione did not exhibit any considerable effect on bomyl degradation. When chloroform extracts were chromatographed, except for unreacted bomyl, there were no phosphorus-containing compounds indicated. Chromatography of the water-soluble fraction showed only dimethyl phosphate (Morello et al., 1968).

BPA [O,O-Dibutyl N-methyl-N-phenyl phosphoramidate]

BPA was incubated with mycelial cells of *Pyricularia oryzae*. Metabolism of BPA was rapid. One compound was identified as the N-demethyl BPA. The other major product was characterized as a hydroxylated product of BPA (Uesugi and Sisler, 1978).

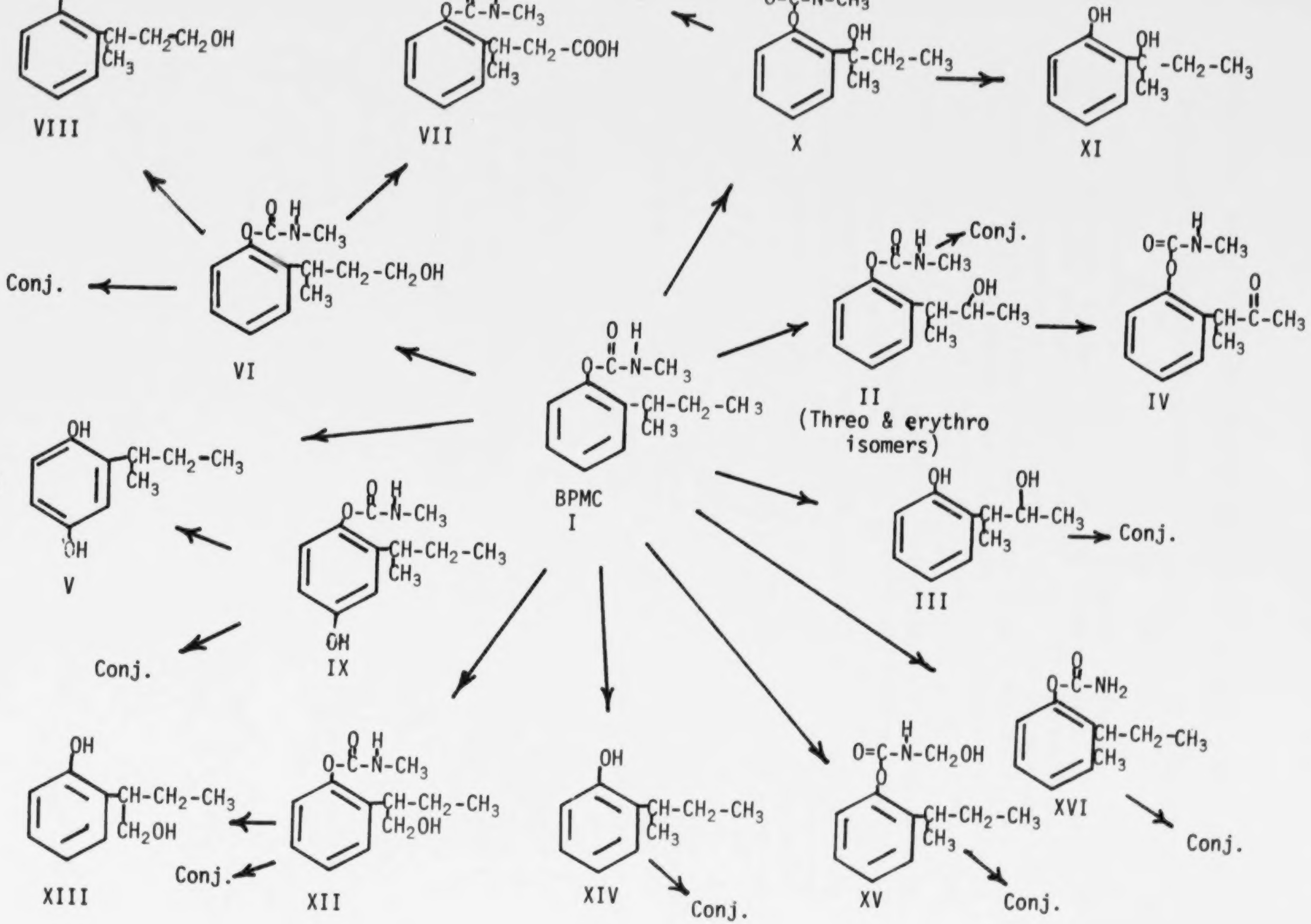
BPMC (Bassa) [2-*sec*-Butylphenyl *N*-methylcarbamate]

When carbonyl-^{14}C BPMC was applied topically to the thoracic region of adult female green rice leafhoppers of Chikugo and Shinwa strains, radioactivity in the water-soluble and unextractable fractions was higher in the Chikuga strain. Penetration rate was the same and the difference was ascribed to differences in metabolism rates (Moriya and Maeda, 1976).

Rice plants were cultured in Wagner's pots until tillering stage and then leaves were treated with ^{14}C-labeled BPMC. Autoradiography after TLC was used to detect the metabolites. Fifteen compounds were identified by co-chromatography with authentic samples. GC-MS was used to identify the main metabolites as compounds II, III, VI, IX, XII, XIV and XV. Hydrolysis of water extracts by β-glucosidase yielded compounds II, IX and XV; hydrolysis by HCl also released III and XVI. In addition to these, compounds IV, V, VII, VIII, X, XI, XIII, XVI, conjugates of II, III, VI, IX, X, XII, XIV, XV and XVI, and 10 unidentified metabolites were also detected. TLC was used to separate degradation products in studies with paddy field soils. Autoradiography detected 22 radioactive compounds. TLC co-chromatography and MS were used to identify the main degradation products as compounds IV, XIV and XVI. Some $^{14}CO_2$ was also observed (Ogawa et al., 1976).

The metabolism of BPMC by the fungus *Aspergillus niger* van Tieghem was also investigated. In addition to unreacted BPMC, metabolites were identified as II (*threo* and *erythro* isomers), IV, VI, X, XII, XIV, XV and XVI. Identification was made with the aid of TLC, IR, MS, NMR and optical rotation and comparisons with authentic samples. The structure of one metabolite was not determined because of insufficient material (Suzuki and Takeda, 1976a and b). Comparative studies with *A. niger*, *Fusarium* sp., *Penicillium funiculosum* Thom, *Cladosporium cladosporioides* (Fres.) de Uries, and *Coniothyrium* sp. indicated quantitative differences primarily. In addition to two unidentified compounds, a third compound observed was believed to be compound VII (Suzuki and Takeda, 1976c). In additional studies with *Cladosporium cladosporioides*, five metabolites were isolated and identified by MS and NMR as metabolites VII, XI, XIV and the *erythro* and *threo* isomers of metabolite II (Suzuki and Takeda, 1976d).

BPMC disappearance in potted soil was faster when as a dust than as a fine granule. The ratio of soil bound residues was higher with fine granule than with dust (Ueji et al., 1978).


VIII
VII
X
XI
Conj.
VI
BPMC
I
II
(Threo & erythro isomers)
IV
V
IX
III
XIII
XII
XIV
XV
XVI
Conj.

BROMOPHOS [*O*,*O*-Dimethyl *O*-(4-bromo-2,5-dichlorophenyl)phosphorothionate]

BROMOPHOS-ETHYL [*O*,*O*-Diethyl *O*-(4-bromo-2,5-dichlorophenyl)phosphorothionate]

Bromophos was enzymatically degraded to 4-bromo-2,5-dichlorophenyl phosphorothionate. This was the only product formed when hog or mouse liver preparations were used. Glutathione stimulated the reaction. When incubated with 4 molar NaOH, dimethyl phosphorothionate formed. No desmethyl bromophos was observed. When incubated with buffers of pH 10 and 11, the aryl phosphorothionate did form (Stenersen, 1969).

The oxon of bromophos was hydrolyzed rather slowly by plasma of sheep, rabbit, rat, and chicken (Machin et al., 1978).

Analyses of meat fats of animals from areas that use bromophos-ethyl dips and sprays to control cattle ticks have detected a residue identified as *O*,*O*-diethyl *O*-(2,5-dichlorophenyl)phosphorothionate (Luke and Dahl, 1976).

BROMOXYNIL [3,5-Dibromo-4-hydroxybenzonitrile]

IOXYNIL [3,5-Diiodo-4-hydroxybenzonitrile]

Microorganisms capable of degradation of bromoxynil and/or ioxynil have been observed in soils (Cullimore and Kohout, 1974). A flexibacterium, strain BR4, degraded bromoxynil with formation of 3,5-dibromo-4-hydroxy-benzamide and -benzoic acid. A third compound was observed. Spectral data indicated a phenol but it was not identified (Smith and Cullimore, 1974).

Using a clay loam soil, ^{14}C-bromoxynil and ioxynil degradation was studied. The half-life was estimated to be 7 days for bromoxynil and 9-10 days for ioxynil. Soil microorganisms used in this study that degraded ioxynil completely to CO_2 or in part did not seem to degrade bromoxynil completely. No metabolites except CO_2 were identified (Hsu and Camper, 1975).

A fungal isolate (*Fusarium solani*) and a gram-negative bacterium (*Klebsiella ozaenae*) degraded ^{14}C-ring-labeled ioxynil with release of $^{14}CO_2$ (Hsu and Camper, 1976). With the fungus in pure culture, ioxynil was degraded into eight products. Two compounds were identified as 3,5-diiodo-4-hydroxybenzamide and its acid analog. $^{14}CO_2$ was formed from both ^{14}CN- and ^{14}C-ring-labeled ioxynil. This was suggestive of ring hydroxylation and fission in accordance with known mechanisms (Hsu and Camper, 1979).

When bromoxynil octanoate was added to clay loam, fen peat and sand soils, residues declined to below the level of detection after 28, 44 and 14 days, respectively (Ingram and Pullin, 1974). In alkaline soils, adsorption of ioxynil occurred. Hydrolysis also occurred to produce 3,5-diiodo-4-hydroxy -benzamide and -benzoic acid. Iodide was also released (Zaki et al., 1967).

BUTACHLOR (Machete) [2-Chloro-2',6'-diethyl-*N*-butoxymethyl)acetanilide]

Soil microorganisms found capable of degrading butachlor included:

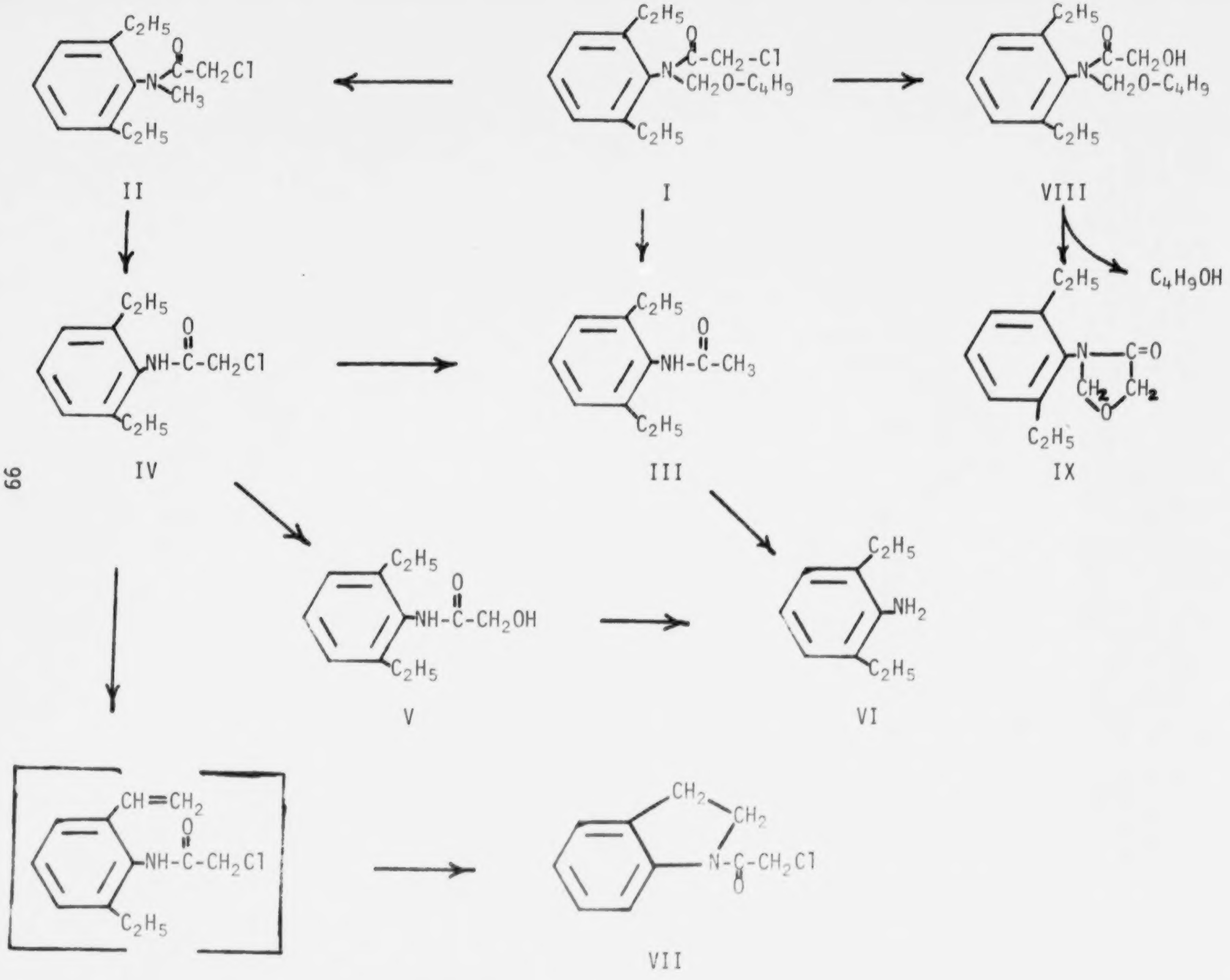
Mucor sufui
Mucor spp. (2)
Penicillium citrinum
Penicillium glaucum
Aspergillus niger
Bacillus subtilis
Fusarium oxysporum
Trichoderma virde
Aspergillus oryzae
Aspergillus usamii
Bacillus megatherium

When butachlor was incubated with *M. sufui* NTU-358, seven metabolites were observed and all but one was characterized:

II. *N*-methyl-2-chloro-2',6'-diethylacetanilide
III. 2',6'-diethylacetanilide
IV. 2-chloro-2',6'-diethylacetanilide
V. 2-hydroxy-2',6'-diethylacetanilide
VI. 2,6-diethylaniline
VII. *N*-chloroacetyl-7-ethyl-2,3-dihydroindole

(Chen, 1978; Chen and Wu, 1978).

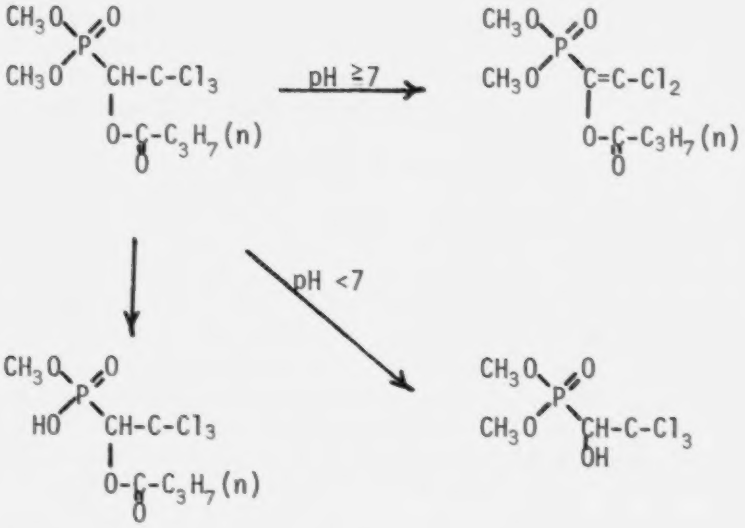
Ultraviolet photodecomposition of butachlor as a thin film on glass was followed with TLC and GLC. The reaction was rapid with a $t_{1/2}$ = 1.5 h and followed first-order kinetics. IR, MS and NMR were used to identify the products. In addition to 2-chloro-2',6'-diethylacetanilide, products characterized were 2-hydroxy-2',6'-diethyl-*N*-butoxymethylacetanilide, 1-chloroacetyl-2,3-dihydro-7-ethylindole, and *N*-(2,6-diethylphenyl)-2,5-dihydrooxazol-4-one (Chen, 1978; Chen and Chen, 1978).



C_2H_5
N
$C(=O)-CH_2Cl$
CH_3
II
$C(=O)-CH_2-Cl$
$CH_2O-C_4H_9$
I
$C(=O)-CH_2OH$
$CH_2O-C_4H_9$
VIII
C_4H_9OH
$NH-C(=O)-CH_2Cl$
IV
$NH-C(=O)-CH_3$
III
$C=O$
CH_2
O
IX
$NH-C(=O)-CH_2OH$
V
NH_2
VI
$CH=CH_2$
$N-C(=O)-CH_2Cl$
VII

BUTONATE [*O*,*O*-Dimethyl 1-*n*-butyrate-2,2,2-trichloroethyl phosphonate]

Metabolism of butonate proceeds via deesterification and by demethylation. In the latter case, ester hydrolysis follows. In the former case, dichlorvos was a minor metabolite. In blood serum of mammals, butonate was metabolized via the vinyl butonate analog and the demethyl vinylbutonate. Methyl phosphate also formed (Dedek and Georgi, 1978).



BUX [3:1 mixture of *m*-(1-Methylbutyl)phenyl *N*-methylcarbamate and *m*-(1-ethylpropyl)phenyl *N*-methylcarbamate]

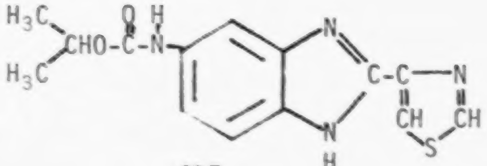
The ^{14}C-labeled methylbutyl isomer of Bux was added to a model ecosystem. At pH 7.9, the half-life was less than four days. After 33 days, algae and *Elodea* plants exhibited residues of about 0.2 to 1 ppm; crabs (*Uca minax*), 0.02-0.08 ppm. Metabolism of Bux was extensive with the formation of conjugates and other polar metabolites, none of which were identified (Yu et al., 1974a).

CAMBENDAZOLE (CBZ) [Isopropyl 2-(4-thiazolyl)-5-benzimidazolecarbamate]

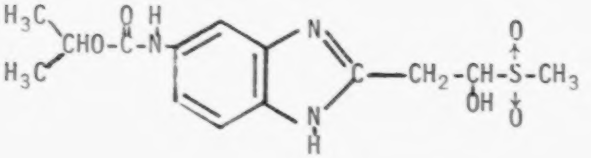
When CBZ was administered to cattle, swine, and sheep, about 14 metabolites were observed in the urine and identified by syntheses and MS. About 20-40% of the dose appeared in the urine. The results of these studies are summarized in the following table.

Animal urine	Compounds isolated
Sheep	II, III, V, VI, VII, IX, XIV, XV
Pig	VIII, XII, XIII, XIV
Cattle	IV, X, XI

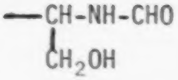
(VandenHeuvel et al., 1978)



CBZ
I



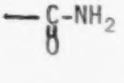
II



$-\underset{\displaystyle CH_2OH}{CH}-NH-CHO$

III

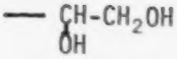
$-CH_2-NH-CHO$ IV



$-\underset{\displaystyle \overset{\|}{O}}{C}-NH_2$

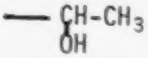
V

$-COOH$ VI



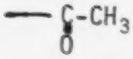
$-\underset{OH}{CH}-CH_2OH$

VII



$-\underset{OH}{CH}-CH_3$

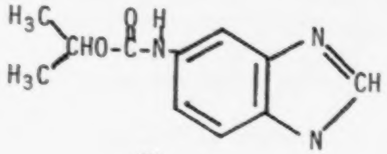
VIII



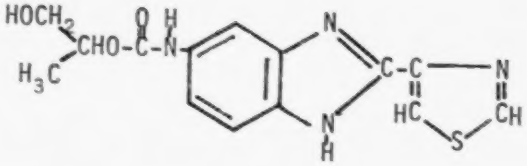
$-\underset{O}{\overset{\|}{C}}-CH_3$

IX

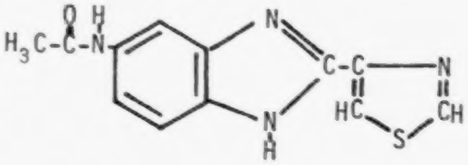
$-CH_2OH$ X



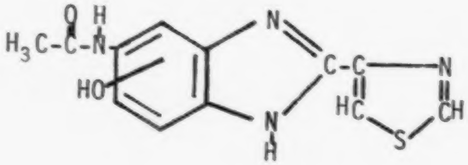
XI



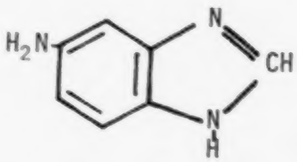
XII



XIII



XIV



XV

CAPTAFOL [N-(1,1,2,2-Tetrachloroethylthio)-4-cyclohexene-1,2-dicarboximide]

In homogenized preparations of vegetables and fruits, captafol decomposed. As the pH value of the preparations increased, decomposition increased. Decomposition was rapid with radish roots, spinach, cucumber, cabbage, muskmelon, satsuma orange peel, greenpepper fruit, potato tuber, and onion; slow in strawberry, tomato, apple and orange. The $t_{1/2} \geq 60$ min in the latter cases. Decomposition appeared to be nonenzymatic. In aqueous solution, in the presence of reduced glutathione and cysteine, the decomposition occurred also (Nutahara and Yamamoto, 1978).

CAPTAN [N-(Trichloromethylthio)-4-cyclohexene-1,2-dicarboximide]

After ^{35}S-captan was administered to rats, almost all of the captan was eliminated via urine and feces within 3 days. A small amount, less than 0.1% of the ^{35}S was incorporated into endogenous compounds or deposited in organs, probably in proteins and nucleic acids. Analyses indicated that a cysteine and glutathione derivative of captan formed (Seidler et al., 1971).

In incubations of captan with rat liver microsomes, drug metabolizing enzyme activity decreased in the presence or absence of NADPH. Some carbonyl sulfide (COS) was observed when NADPH was present. Although not observed, the formation of thiophosgene ($CSCl_2$) was suggested since $CSCl_2$ hydrolyzes rapidly to produce COS (Peeples and Dalvi, 1978).

In water, captan half-life is maximally about 710 minutes. The hydrolytic products included 4-cyclohexene-1,2-dicarboximide, CO_2, HCl, and sulfur (Wolfe et al., 1976a).

When captan was reacted with glutathione, the major product observed was oxidized glutathione. With all or a portion of the $-S-C-Cl_3$ released from captan, a series of compounds were formed with GSH (Siegel, 1970).

CARBARYL (Sevin) [*N*-Methyl naphthyl-1-carbamate]

Liver tissue from man, rat, guinea pig and dog was incubated with carbaryl. Identified metabolites were the same in each case: naphthyl sulfate, naphthyl glucuronide, hydroxycarbaryl sulfate, hydroxycarbaryl glucuronide, and 5,6-dihydro-5,6-dihydroxycarbaryl glucuronide. Three compounds were not identified (Sullivan et al., 1972).

Studies with perfused lung tissue indicated that lungs were able to take up carbaryl and metabolize it. Metabolism was rapid with over 22% of the dose metabolized within 15 min. Only α-naphthol and 4-hydroxycarbaryl were identified (Blase and Loomis, 1976).

Bean plants were treated with carbaryl and the bound residues were fed to rats. About 98% of the dose was eliminated in feces within 48 h. Urinary excretion amounted to 1.3% (Marshall and Dorough, 1977).

Using rat tissue fractions, carbaryl metabolism was greater in the hepatic microsomal fractions than in any other preparation. 1-Naphthol was the major metabolite in all rat tissue fractions. The major carbaryl metabolite with quail preparations was also 1-naphthol. However, in the postmitochondrial fraction of liver, 1-naphthyl-*N*-hydroxymethyl carbamate and 1-naphthol were both produced (Hinderer, 1975; Hinderer and Menzer, 1976b). With carbaryl and rat blood, lung, kidney and testis tissues, 1-naphthol, 5-HO-carbaryl, hydroxymethylcarbaryl, and two unknowns were formed; with liver, 4-hydroxycarbaryl and 5,6-dihydro-5,6-dihydroxycarbaryl were also observed (Hinderer and Menzer, 1976a).

In rainbow trout (*Salmo gairdneri*), carbaryl gave rise to 1-naphthyl glucuronide and 5,6-dihydro-5,6-dihydroxycarbaryl (Statham et al., 1975).

Larvae of the European corn borer [*Ostrinia nubilalis* (Hubner)] were exposed to carbaryl. Hydroxymethylcarbaryl was the main metabolite with some 5,6-dihydro-5,6-dihydroxycarbaryl also formed. Water soluble metabolites consisted of glucuronides and/or sulfates of hydroxymethyl-, 4-hydroxy-, 5-hydroxy-, and 5,6-dihydro-5,6-dihydroxy- carbaryl and 1-naphthol. *In vitro* ether soluble metabolites included 4-hydroxy-, 5-hydroxy-, *N*-hydroxymethyl-, and 5,6-dihydrodihydroxy-carbaryl (Kuhr and Davis, 1975).

Male and female cockroaches (*Periplaneta americana*, *Leucophaea maderae*, and *Gromphadorhina portentosa*) and the locust (*Schistocerca gregaria*) decarbamoylated carbaryl releasing CO_2 (Cocks, 1975).

Larvae of resistant *Anopheles albimanus* metabolized carbaryl to *N*-hydroxymethylcarbaryl, the 5,6-dihydrodihydroxycarbaryl and an unidentified metabolite (Ariaratnam and Georghiou, 1975). In the alfalfa leafcutting bee [Megachile pacifica (Panzer)], carbaryl was hydroxylated at the 4, 5 and 5+6 positions. Some hydrolysis to 1-naphthol occurred. Hydrolysis of water soluble conjugates gave 1-naphthol, N-hydroxymethylcarbaryl, 5-hydroxycarbaryl, 5,6-dihydro-5,6-dihydroxycarbaryl and carbaryl (Guirguis, 1975).

In flies, 1-naphthol was converted to 1-naphthylglucoside-6-phosphate (Heenan and Smith, 1967). Similar results were observed with blowflies and New Zealand grass grubs (Binning et al., 1967).

Tobacco cells in suspension culture were incubated with ^{14}C-carbaryl labeled in the C_1-naphthyl, carbonyl, or N-methyl position. About 18% of the characterized metabolites was in the form of N-hydroxymethylcarbaryl, which was excreted by the cells into the culture medium. Within the cells, the metabolites consisted mostly of conjugates of 1-naphthol (about 73% of characterized metabolites), N-CH_2OH-carbaryl, 7-hydroxycarbaryl, 4-hydroxycarbaryl, 5-hydroxycarbaryl. A new type of plant conjugate was identified as O-1-naphthylcholesterol (cholest-5-en-3β-yl-1-naphthol). An unconjugated metabolite was tentatively identified as 1,4-dihydro-1,4-epiperoxynaphthalene. Not completely characterized but also observed was a β-glucosidase-resistant conjugate of a cis-dihydrodiol (Locke et al., 1976).

The rate of dissipation of carbaryl from soils varied from 3 to 70% disappearance of radioactivity after 4 days. Carbon dioxide was formed by attack on the ring. Hydroxymethylcarbaryl was formed by a fungus SF-10 and P. implicatum. P. lilacinum and A. elegans produced small amounts of 5,6-dihydro-5,6-dihydroxycarbaryl (Rodriguez and Dorough, 1977).

Isolated marine organisms degraded carbaryl and 1-naphthol. Metabolites were not identified (Sikka et al., 1975). When a Pseudomonas sp. was incubated with 1-naphthol, a dihydrodihydroxy-1(2H)-naphthalenone was observed. Of two structures, the spectral information favored 2,3-dihydroxy-3,4-dihydro-1(2H)-naphthalenone (Walker et al., 1975b). An enzyme was isolated from the fungus Rhizoctonia praticola and incubated with 1-naphthol. MS spectra indicated polymerization to at least a pentameric compound. A tetramer, one trimer and two dimers were purified from the mixture. One dimer was identified as 4,4'-bi-1-naphthol (Sjoblad, 1977; Sjoblad et al., 1976).

Carbaryl was irradiated at $\lambda > 265$ nm in various solvents. In all cases, 1-naphthol was formed and in cyclohexane it was the only product. In polar solvents (i-propanol, t-butanol, ethanol), small amounts of naphthamides, naphthalene and β-naphthyl-1-naphthol were also produced (Addison et al., 1975). The photolysis half-life for carbaryl in sunlight was 6.6 days in distilled water (Wolfe et al., 1978).

In aqueous media, a number of carbaryl decomposition products were present within 7 days; and, by the 19th day, 13 spots were visible in chromatographs of suspensions of pH 5-10, stored at 37C (Maruszewska and Gertig, 1977). In other studies, carbaryl $t_{1/2}$ varied from 0.15 days at pH 9 to 1500 days at pH 5 (Wolfe et al., 1978).

CARBOFURAN (Furadan) [2,2-Dimethyl-2,3-dihydrobenzofuranyl-7-N-methylcarbamate]

When carbofuran was added to a model ecosystem, hydrolysis ensued rapidly to produce the phenol analog and N-methylcarbamic acid. The latter degraded rapidly to CO_2 and other compounds. 3-Ketocarbofuran, 3-hydroxycarbofuranphenol, N-hydroxymethylcarbofuran and 3-hydroxycarbofuran were also observed (Yu et al., 1974). In the freshwater clam Elliptio, injected carbofuran was rapidly excreted as a conjugate that was refractive to hydrolysis by glucosidases and other hydrolases but not 0.5 N HCl (Robinson and Fisher, 1978).

Carbofuran was applied to strawberries and berries and leaves were sampled. Residue analyses indicated the presence of 3-ketocarbofuran and the 3,7-diol (3-hydroxycarbofuranphenol) (Archer et al., 1977). In maize plants (Zea mays L.) treated with carbofuran, the major metabolite was 3-hydroxycarbofuran. Hydrolysis of the organosoluble plant extract also gave carbofuranphenol and 3-hydroxycarbofuranphenol, indicating the presence of glycosidic conjugates. There was an indication of the presence of 3-ketocarbofuranphenol (Kapoor and Kalra, 1975).

Carbofuran was applied with carrot seed at time of planting. The carrot plants were treated at several intervals and then removed for analysis. Little or no parent compound was found. The 3-hydroxycarbofuran was found primarily in peel of the top 3 cm of the carrot (Finlayson et al., 1976). When carbofuran was applied to radishes, it was rapidly bound in the tissues. Hydrolysis by enzymes and HCl only released 5 to 15% of the bound residues. The aglycones were identified as carbofuran and 3-hydroxycarbofuran (Wheeler et al., 1978). When corn was treated with carbofuran, more than 90% of the carbofuran was metabolized to 3-hydroxy- and 3-oxo- carbofuran. The 3-hydroxycarbofuran comprised more than 80% of the metabolite residue. Most of the residue was in the leaves. Lesser amounts were in cob and stalk and only trace amounts were in the grain. Unchanged carbofuran predominated in the cob and stalk (Turner and Caro, 1973).

When applied to soybean foliage, carbofuran gave rise to 3-hydroxycarbofuran which was observed in extracts of seeds. In mungbean plants exposed to carbofuran, the 3-hydroxy- and 3-keto- carbofuran were observed in the leaves and the 3-hydroxycarbofuran in seeds (Talekar et al., 1977). Metabolism of carbofuran by bean plants produced some water-soluble conjugated metabolites, including 3-hydroxycarbofuran glucoside and some carbofuran phenolic derivatives. When these conjugates were fed to rats, the 3-hydroxycarbofuran glucoside was cleaved at the glucoside linkage. The carbamate ester was hydrolyzed and the 3-hydroxy was oxidized to the 3-keto form. The free hydroxy groups formed by hydrolysis of glucosides were in part conjugated again as glucuronides before being excreted (Marshall and Dorough, 1977).

In addition to unchanged carbofuran, residues of the 3-hydroxy analog were observed in mushrooms (Agaricus bisporus) when cultivated in soil to which carbofuran had been added (Kalberer and Vogel, 1978).

House crickets (Acheta domesticios L.) were exposed to atrazine and then to carbofuran. Carbofuran phenol, 3-hydroxycarbofuran and two unidentified metabolites were observed. Controls exhibited a statistically higher percentage of hydroxylated compounds than did those pre-exposed to atrazine. Carbofuran degradation was apparently inhibited at the level of carbon-3 hydroxylation (Chio and Sanborn, 1977).

Carbofuran was incorporated in soils and its disappearance monitored. Disappearance of 95% of carbofuran varied between 145 and 434 days as a function of temperature, moisture, and soil pH and followed first-order kinetics (Caro et al., 1976).

In soils containing high levels of actinomycetes, carbofuran degradation was rapid. At 20C, about 50% was gone within approximately 4 weeks. 3-Hydroxycarbofuran incubated in soil under similar conditions was not detectable after 4 weeks (Williams et al., 1976). Carbofuran degradation was most rapid in soils under flooded conditions. A bacterium, not identified, was isolated from flooded soil and found capable of degrading carbofuran under static conditions (Venkateswarlu et al., 1977).

Carbofuran hydrolyzed, primarily chemically, to the phenol in 5 days in paddy water. While autoclaving did not affect the hydrolysis, further degradation was inhibited (Siddaramappa et al., 1978). In flooded soils, under anaerobic conditions, carbofuran phenol and 3-hydroxycarbofuran accumulated. In aerobic soils, these compounds did not accumulate (Venkateswarlu and Sethunathan, 1978). The hydrolysis $t_{1/2}$ in rice paddy water was 1.2 h at pH 10 and 864 h at pH 7 (Seiber et al., 1978).

Alfalfa stalks were cut, sprayed with a Furadan 4 Flowable aqueous formulation, dried in the dark, and then exposed to artificial UV irradiation (GE germicidal lamps - G15T8). 3-Hydroxycarbofuran increased most dramatically in the dark. In these studies, 3-ketocarbofuran, 3-hydroxycarbofuran, 3,7-diol, and 3-keto-7-phenol increased. Maximum loss of all compounds occurred after about 10 days exposure (Archer, 1976).

Pyrolysis in a horizontal quartz tube, with a movable variable temperature oven, closely appropximated mainstream smoke resulting from burning cigarettes. When carbofuran was added to the cigarette, carbofuran phenol and 2-methyl-7-benzofuranol were observed in about 90% yield. The remainder consisted of three unidentified materials, CH_4, CO, CO_2 and methyl isocyanate (Atallah et al., 1975).

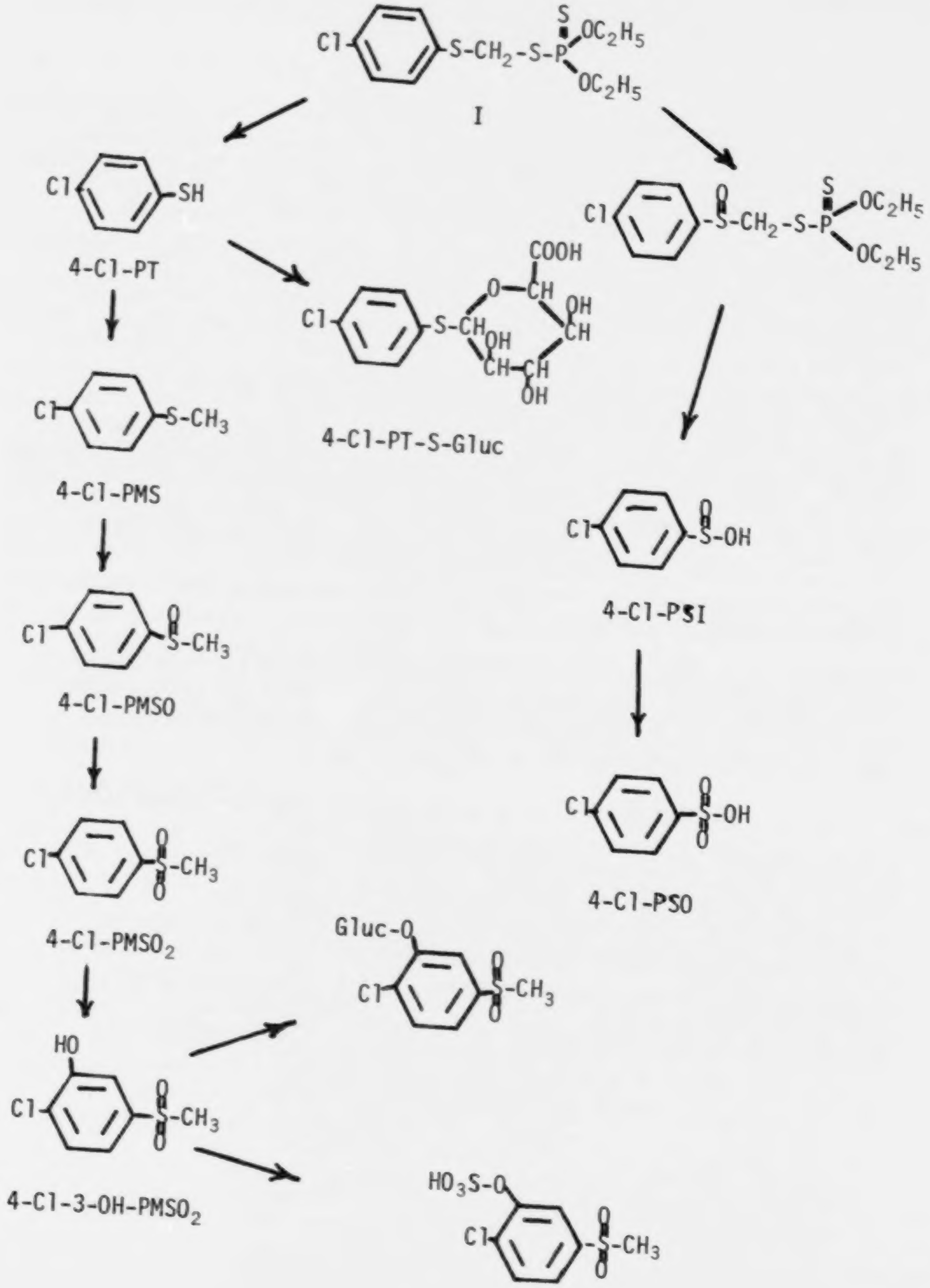
CARBOPHENOTHION (Trithion; *O*,*O*-Diethyl *S*-(4-chlorophenylthiomethyl) phosphorodithioate) [*S*-(4-Chlorophenylthiomethyl) *O*,*O*-diethyl phosphorodithioate]

Within 96 h after administration of ^{14}C-phenyl-labeled carbophenothion and carbophenothion sulfoxide to rats 71-80% of the radioactivity appeared in the urine. Analyses indicated a similar metabolic pattern for both compounds, qualitatively and quantitatively. Metabolites identified by MS included 4-ClPMSO$_2$, 4-Cl-3-OHPMSO$_2$ (free and conjugated), 4-ClPSO, and 4-ClPSI. ClPT, conjugated, and ClPTS were also present. When [thiomethyl-^{14}C]trithion was used, ^{14}CO$_2$ was produced. No S-methylated metabolites were observed, indicating that the methyl group of 4-ClPMSO$_2$ arose from endogenous sources and not from the trithion methylene group. Presence of 4-ClPTS-gluc after trithion sulfoxide administration indicated reduction of the sulfoxide. Differences were noted when 4-chlorothiophenol (4-ClTP) was administered. *In vitro* studies with rat liver homogenates gave evidence that the sulfoxide was reduced to carbophenothion. Other metabolites included 4-ClTP, probably arising from carbophenothion cleavage; 4-ClPMSO and its 3-glucuronide analog; 4-ClPSI; and 4-ClPSO (DeBaun and Menn, 1976; Menn et al., 1974). In other studies, after male Sprague-Dawley rats were administered carbophenothion by gavage, analysis of urine showed the presence of diethyl phosphate, diethyl phosphorothioic acid, and 4-chlorothiophenol (Bradway et al., 1977).

[^{14}C]4-Chlorothiophenol (4-ClTP) was administered to male Simonsen rats. Metabolites were separated by TLC, located by autoradiography and identified by cochromatography with authentic standards. In some cases MS was also used.

Metabolite	Identification Method
4-Chlorophenyl methyl sulfone (4-ClPMSO$_2$)	GLC, MS
4-Chloro-3-hydroxyphenyl methyl sulfone (4-Cl-3-OHPMSO$_2$)	GLC, MS
O-Sulfate ester of 4-Cl-3-OHPMSO$_2$	Cochromatography
4-Chlorobenzenesulfonic acid (4-ClPSO)	GLC, Cochromatography
4-Chlorophenylthio-*S*-glucosiduronic acid (4-ClPT-S-gluc)	Cochromatography, two dimensional TLC, MS
Glucuronide of 4-Cl-3-OHPMSO$_2$	Cochromatography

(Menn et al., 1974)


I
4-Cl-PT
4-Cl-PT-S-Gluc
4-Cl-PMS
4-Cl-PMSO
4-Cl-PMSO2
4-Cl-3-OH-PMSO2
4-Cl-PSI
4-Cl-PSO
Gluc-O
HO3S-O

CARBOXIN (Vitavax, DCMO, 5,6-dihydro-2-methyl-1,4-oxathiin-3-carboxanilide) [2,3-dihydro-5-carboxanilido-6-methyl-1,4-oxathiin]

OXYCARBOXIN (Plantvax) [2,3-dihydro-5-carboxanilido-6-methyl-1,4-oxathiin-4,4-dioxide]

A *Nocardia* sp., capable of using acid anilides as a sole source of carbon, was isolated from soil. Degradation was initiated by amide hydrolysis. This was followed by oxidation of the aniline moiety via pyrocatechol and the β-ketoadipate pathway. The acid moiety accumulated in the incubation medium (Bachofer, 1976; Bachofer et al., 1973).

Rhizopus japonicus degraded carboxin to a substituted acid anilide (Wallnofer, 1968). When incubated with *B. sphaericus*, carboxin gave rise to aniline (Wallnofer and Engelhardt, 1971).

When bean plants were exposed to oxycarboxin, four degradation products found in the plants and solution in which the plants were incubated were identified as:

1. 2-(2-hydroxyethylsulfonyl)acetanilide
2. 4-phenyl-3-thiomorpholinone-1,1-dioxide
3. 2-(vinylsulfonyl)acetanilide

(Bates, 1973).

CARTAP [1,3-Bis-(carbamoylthio)-2-(*N*,*N*-dimethylamino)propane]

In aqueous medium, cartap hydrochloride (I) hydrolyzed with loss of two $-H_2N-C=O$ to yield the 1,3-dimercapto-2-(*N*,*N*-dimethylamino)propane (II). The latter oxidizes readily to the cyclic disulfide, 4-(*N*,*N*-dimethylamino)-1,2-dithiolane (III). At pH 7 and 25C, the half-life of cartap HCl was 10 minutes. The $t_{1/2}$ for compound III (nereistoxin) was calculated to be 2.4 years at pH 7. At pH 1.1 and 100C, the $t_{1/2}$ was 2.2 h and the hydrolysis product was 2-(*N*,*N*-dimethylamino)-3-mercaptopropanesulfenic acid (IV) (Asahi and Yoshida, 1977).

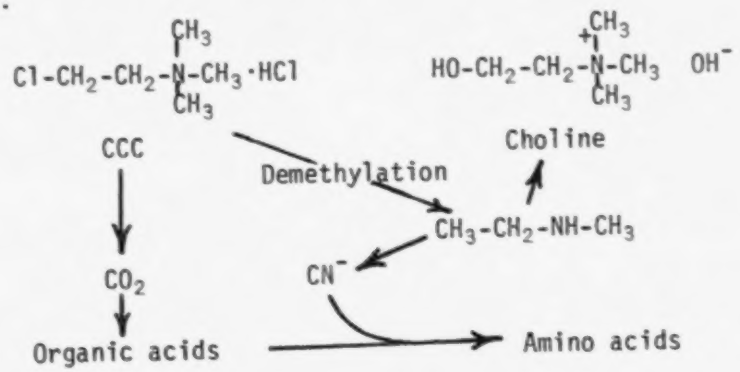
CCC (Chlormequat, Cycocel, Chlorocholine chloride) [2-Chloroethyl trimethylammonium chloride]

When ^{14}C-labeled CCC was applied to kohlrabi, cauliflower, or tomatoes, degradation of CCC was very small. The first product was probably choline which entered the plant pool. Small amounts of labeled methyl groups from choline were found as S-methyl methionine (Muller and Schuphan, 1975). CCC was not degraded when applied to sugarcane (Marei et al., 1975). In alfalfa, CCC was slowly metabolized and was primarily incorporated into choline of phosphatidylcholine (Willemot and Belzile, 1970).

Almond seedlings were treated with labeled CCC. Translocation to leaves and to the roots was observed. $^{14}CO_2$ was formed within 2 h after application. Radioactivity was observed in 17 known amino acids, an unidentified ninhydrin positive compound, malic acid, citric acid, choline and 2-chloroethylamine (Intrieri and Ryugo, 1974).

Studies with soil microorganisms indicated that CCC breakdown occurred through oxidative processes. When CCC was incubated in rumen contents or juice under anaerobic conditions, microbial degradation of CCC did not occur (Ackerman and Lexow, 1975).

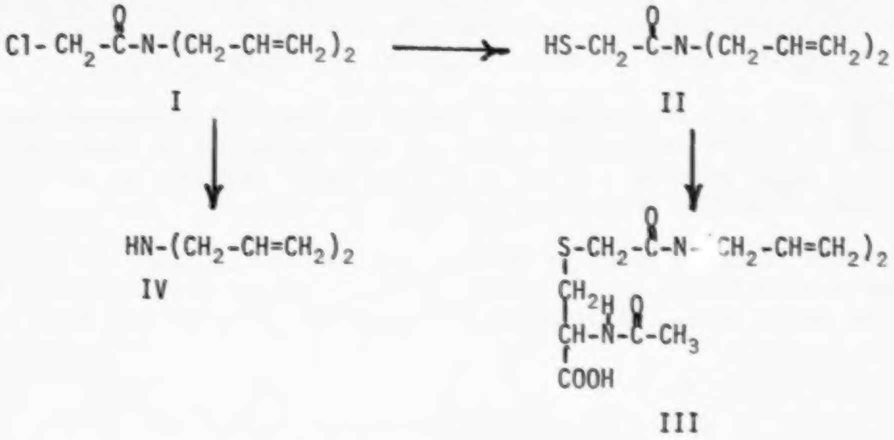
When added to dough prior to baking, most of the CCC and its degradation products volatilized into the air. A small amount that decomposed to choline chloride and other materials remained (Schuler and Merbach, 1978).



CDAA [N,N-Diallyl-2-chloroacetamide]

When [^{14}C]CDAA was fed to rats, more than 80% of the ^{14}C was excreted via urine within 48 h. The major metabolite was identified as the mercapturic acid analog (III). Compounds II and IV were also identified. Several other compounds were observed but not characterized (Lamoureux and Davison, 1975).

In plants, CDAA forms a GSH conjugate but this does not seem to be metabolized to the mercapturic acid (Shimabukuro et al., 1977).



$$Cl-CH_2-\overset{O}{\overset{\|}{C}}-N-(CH_2-CH=CH_2)_2 \longrightarrow HS-CH_2-\overset{O}{\overset{\|}{C}}-N-(CH_2-CH=CH_2)_2$$

$$HN-(CH_2-CH=CH_2)_2$$

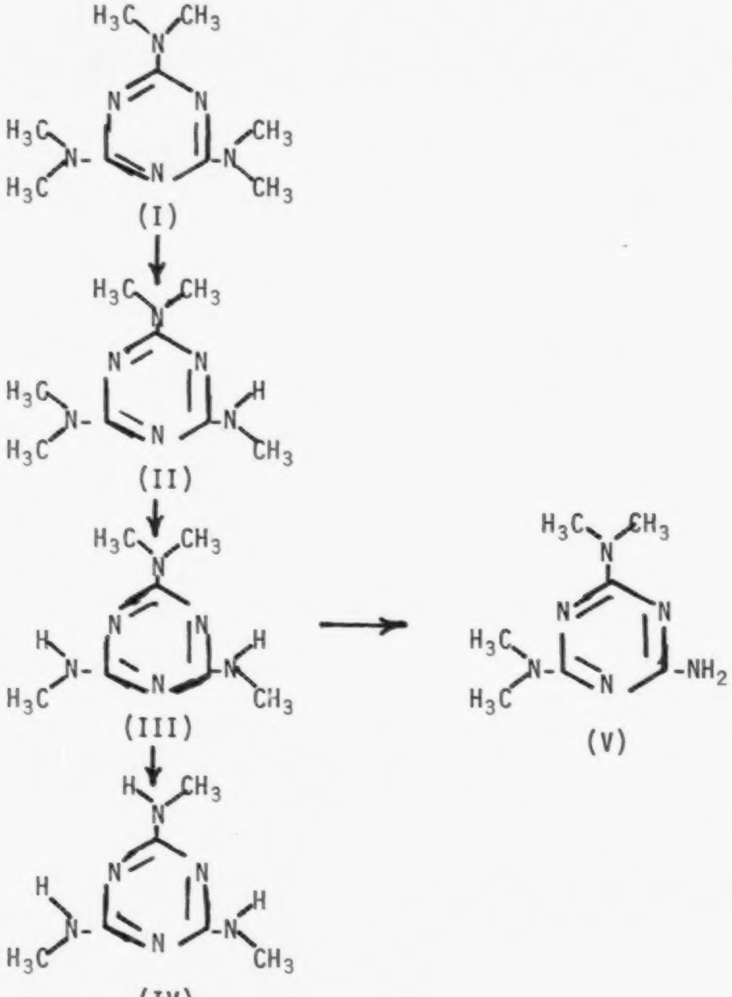
$$S-CH_2-\overset{O}{\overset{\|}{C}}-N-(CH_2-CH=CH_2)_2, \quad S-CH_2-CH(COOH)-\overset{H}{N}-\overset{O}{\overset{\|}{C}}-CH_3$$

ENT-51007 [*N*,*N*,*N*',*N*'-Tetramethyl-*p*-piperidinophosphonic diamide]

Regardless of the method of application to boll weevils (*Anthonomus grandis* Boheman), most of the ENT-51007 disappeared after 24 h (Terranova, 1969).

HEMEL (N^2,N^2,N^4,N^4,N^6,N^6-Hexamethylmelamine) [2,4,6-Tris(dimethylamino)-*s*-triazine]

Houseflies degraded hemel (I) via step-wise demethylation to form pentamethylmelamine (II), N^2,N^2,N^4,N^6-tetramethylmelamine (III), N^2,N^4,N^6-trimethylmelamine (IV), and N^2,N^2,N^4-trimethylmelamine (V). After extraction of excreta and preparative TLC, identification was made by GLC, UV and IR. No mono- or di-methylmelamines, melamine, nor N^2,N^2,N^4,N^4-tetramethylmelamine were found. Some CO_2 was also observed (Chang et al., 1968).



CHEMOSTERILANTS

HEMPA (HMPA) [Hexamethylphosphoramide]

THIO-HMPA [Hexamethylthiophosphoramide]

PMPA [Pentamethylphosphoramide]

In mice and rats administered HMPA, the pentamethyl-, tetramethyl-, and trimethylphosphoramides were isolated and identified. *In vitro* studies with rat liver slices indicated that demethylation proceeded via oxidation of the methyl group to formaldehyde. The latter was trapped and precipitated with dimedone (Jones and Jackson, 1968).

Mice and rats metabolized thio-HMPA to thio-PMPA and HMPA. Demethylation of the latter gave rise to PMPA. The latter also arose from thio-PMPA through a S-O exchange (Jones and Jackson, 1968).

Studies with hexa-alkylphosphoramides (ethyl and propyl) were conducted. the N^1,N^2,N^3-tri-alkylphosphoramides were found in urine of rats administered the hexalkylphosphoramides (Jones and Jackson, 1968).

TLC, GLC, and radiochromatography were used to identify hempa and its major metabolite pentamethylphosphoric triamide (PMPT) in extracts of treated flies and their excreta. Some CO_2 was also formed (Chang et al., 1967). The same metabolite was obtained *in vitro* with a house fly abdomen microsomal system. This system required NADPH and oxygen (Akov et al., 1968). It was also observed that carbamate-resistant house flies metabolized hempa more rapidly than did susceptible flies (Akov and Borkovec, 1968). Other studies indicated the presence of four metabolites. Three were identified with the aid of TLC, radiochromatograms and IR as PMPT, *N*,*N*,*N'*,*N"*-tetramethylphosphoric triamide, and *N*,*N'*,*N"*-trimethylphosphoric triamide. Some CO_2 also was produced (Chang and Borkovec, 1969).

When ^{14}C-hempa was ingested by adult boll weevils (*Anthonomus grandis* Boheman), hempa was metabolized rapidly. In addition to unchanged hempa, excreta contained 10 decomposition products. Of these, four were identified as triamide analogs: pentamethyl; *N*,*N*,*N'*,*N'*-tetramethyl; *N*,*N*,*N'*,*N"*-tetramethyl; and *N*,*N'*,*N"*-trimethyl. Some $^{14}CO_2$ was also expired (Bull and Borkovec, 1973).

CHEMOSTERILANTS

METEPA (Methaphoxide) [Tris(2-methyl-1-aziridinyl)phosphine oxide]

Larvae and adults of the mosquito (*Culex tarsalis* Coquillett) degraded METEPA within 48 h of administration. Adult houseflies (*Musca domestica* L.) degraded this compound within 2 h. Houseflies and mice produced a major breakdown product believed to be phosphoric acid. *In vitro* studies showed METEPA was stable in alkaline solution but not in acidic solution. In 1N alkali, 50% hydrolysis required more than 100 h; in 1N acid, the time required was less than one minute (Plapp et al., 1962). The principal metabolite produced by screw-worm fly (*Cochliomyia hominivorax* Coquerel) and stable fly *Stomoxys calcitrans* L.) was inorganic phosphate (Chamberlain and Hamilton, 1964).

CHEMOSTERILANTS

TEPA (APO, Aphoxide, Triethylene phosphoramide) [Tris(1-aziridinyl) phosphine oxide]

THIOTEPA (Triethylene thiophosphoramide) [Tris(1-aziridinyl)phosphine sulfide]

Humans, administered TEPA, metabolized this compound to inorganic phosphate and an organic phosphorus compound not identified (Nadkarni et al., 1959). Similarly inorganic phosphate was observed after TEPA administration to Wistar rats (Craig and Jackson, 1955) and mice (Jones and Jackson, 1968; Nadkarni et al., 1957). The organic compound observed also gave rise to inorganic phosphate and was probably an intermediate between TEPA and phosphate.

When applied to houseflies, TEPA was present unchanged or as unidentified metabolites in the treated flies. Excreta contained no metabolites with the aziridinyl group. Some CO_2 was observed (Chang et al., 1966). More than 90% of TEPA applied to fall armyworm moths disappeared within 24 h. No metabolites were found (Cox et al., 1967). Within 24 h after treatment of adult mosquitoes (*Culex pipiens fatigans*) as pupae with TEPA and thiotepa, no detectable chemosterilant was present in their tissue (Labrecque et al., 1972).

Thiotepa was administered to German cockroach (*Blattella germanica* L.), housefly (*Musca domestica* L.), and stable fly (*Stomoxys calcitrans* L.). The only metabolite observed was TEPA, the oxygen analog of thiotepa (Parish and Arthur, 1965).

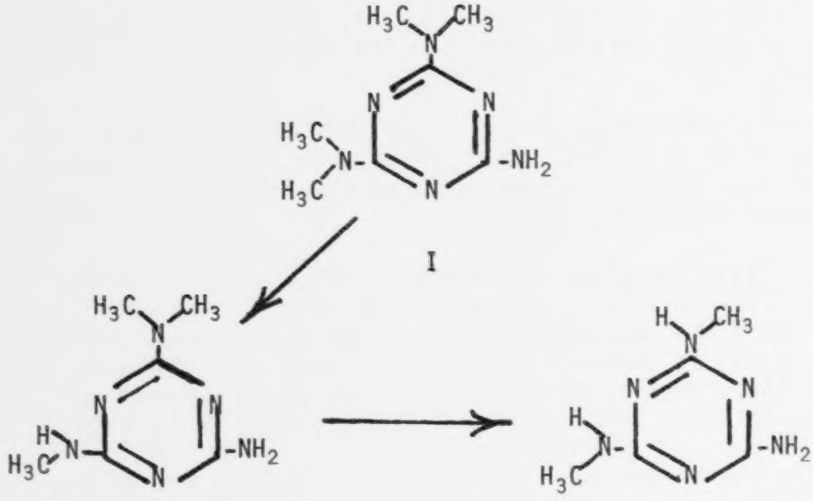
In acidic or neutral solutions, TEPA degradation yielded ethylenimine. Stability of TEPA and ethylenimine was found to be pH dependent. Cleavage of the C-N bond was also indicated (Beroza and Borkovec, 1964).

TMAC [*N*,*N*'-Tetramethylenebis(1-aziridinecarboxamide]

TMAC was rather persistent in insects with about 25% of a topical application to the black blow fly [*Phormia regina* (Meigen)] still present after 504 h. Stability in aqueous solutions, however, was not good (Terranova and Crystal, 1970).

TMM (*N*^{2},*N*^{2},*N*^{4},*N*^{4}-Tetramethylmelamine) [2-Amino-4,6-bis(dimethylamino)-*s*-triazine]

TMM (I) was injected into male *Musca domestica* L. In addition to CO_2, other metabolites observed and identified with TLC, UV, IR and GC included desmethyl-TMM (II) and *N*^{2},*N*^{4}-di-desmethyl-TMM (III). Other unidentified compounds were present (Chang et al., 1970).


H3C
CH3
N
N
N
H3C
N-
-NH2
H3C
N
H3C
CH3
N
N
N
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N-
-NH2
H3C
N
H
CH3
N
N
N
H
N-
-NH2
H3C
N

I

II

III

CHC [Cyclohexanecarboxylic acid]

^{14}C-Cyclohexanecarboxylic acid was administered via duodenal cannula to male Wistar rats. The radioactivity was eliminated very rapidly via bile and urine. TLC, radioautography, mass spectrometry and proton magnetic resonance spectrometry were used to isolate and identify the metabolites. Excretion of metabolites was primarily in urine as hippurate, and the β-glucuronides of benzoic and cyclohexanecarboxylic acids (Brewster et al., 1977a). When perfused rat livers were used, metabolism of cyclohexanecarboxylic acid was similar to that observed *in vivo*. Only the benzoyl glucuronide was not observed *in vitro* (Brewster et al., 1977b).

Rabbits received CHC orally or subcutaneously. Within 24 h, CHC appeared in urine as the hippurate (Dickens, 1947). Similarly, a dog fed CHC, excreted the hippuric acid analog in urine (Friedmann, 1911; Bernhard, 1937).

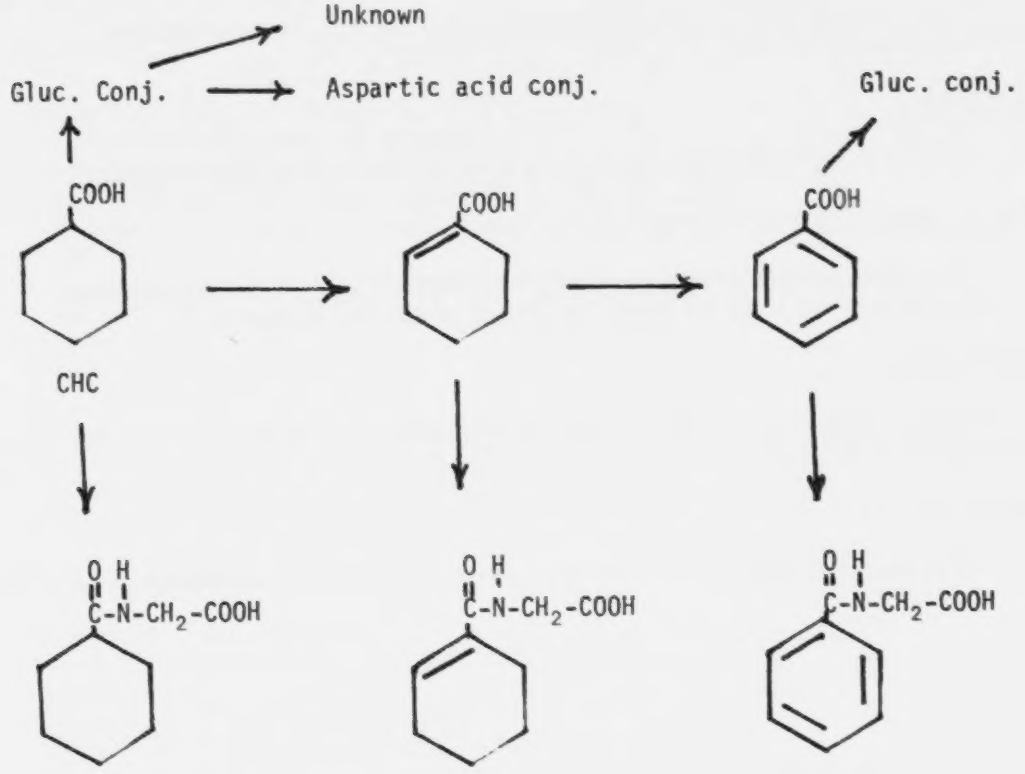
An enzyme, isolated from guinea pig liver and liver mitochondria, catalyzed the aromatization of CHC. Incubation of CHC-CoA produced cyclohexene-1-carboxyl-CoA and benzoyl-CoA plus one unidentified compound (Babior and Bloch, 1966).

Bean plants, *Phaseolus vulgaris*, were treated with CHC. Analyses indicated that in addition to unchanged CHC, 1-cyclohexanecarbonyl-β-D-glucose and *N*-cyclohexanecarbonyl-L-aspartic acid were present. The latter apparently formed from the glucoside. The glucoside also seemed to be the precursor of a third metabolite not identified (Padmanabhan and Wort, 1977; Severson, Jr., et al., 1970).

Of 33 isolated microorganisms capable of using CHC as a sole source of carbon, 32 metabolized CHC by -oxidation of the CoA ester. The one strain which did not was classified as an *Alcaligenes* strain. This was capable of rapidly oxidizing *trans*-4-HO-CHC, 4-keto-CHC, *p*-HO-benzoate, and protocatechuate. In these studies, it was observed that hydroxylation of CHC occurred at the 4-position. The data were consistent with a pathway from CHC to *trans*-4-HO-CHC to 4-keto-CHC to *p*-hydroxybenzoate and then *meta*-fission and oxidation via the 2-HO-4-carboxymuconic semialdehyde path (Taylor and Trudgill, 1978).

A bacterium, designated as PRL W19, metabolized CHC via classical β-oxidation of CoA intermediates. The proposed pathway was CHC → CHC-CoA → cyclohexene-1-carboxyl-CoA → *trans*-2-HO-CHC-CoA → 2-keto-CHC-CoA → pimelyl-CoA → → glutaryl-CoA → glutaconyl-CoA → crotonyl-CoA → β-HO-butyryl-CoA → acetoacetyl-CoA → acetyl-CoA (Blakely, 1978).

Arthrobacter sp. metabolized CHC via t-4-hydroxycyclohexanecarboxylic acid (TCHC), 4-ketocyclohexanecarboxylic acid (4-KCHC), 4-hydroxybenzoic acid, protocatechuic acid, and β-ketoadipic acid. The conversion of TCHC to 4-KCHC required NAD (Blakley, 1974). A bacterium, identified as Acinetobacter anitratum, metabolized CHC to cyclohex-1-ene-1-carboxylate, 2-HO-CHC and pimelate (Rho and Evans, 1975).


Unknown
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Aspartic acid conj.
Gluc. conj.
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COOH
COOH
CHC
O H
C-N-CH$_2$-COOH
O H
C-N-CH$_2$-COOH
O H
C-N-CH$_2$-COOH

Chlordane and Related Compounds

α - (or cis-) chlordane

1-exo,2-exo,4,5,6,7,8,8-octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene

γ- (or trans-) chlordane

1-exo,2-endo,4,5,6,7,8,8-octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene

Chlordene

4,5,6,7,8,8-hexachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene

Chlordene epoxide

4,5,6,7,8,8-hexachloro-exo-(cis)-2,3-epoxy-3a,4,7,7a-tetrahydro-4,7-methanoindene [also an endo-(trans)-2,3-epoxy- isomer].

Oxychlordane

1-exo,2-endo,4,5,6,7,8,8-octachloro-2,3-exo-epoxy-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene

Heptachlor

1,4,5,6,7,8,8-heptachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene

CHLORDANE

CHLORDENE

Cis- and *trans*-chlordane were administered in oil to rats. After *extraction* and clean-up on florisil and silicic acid, TLC was used to purify the metabolites and GLC and MS were used to identify them. Excretion of ^{14}C-compounds was more rapid after *cis*-chlordane treatment than after *trans*-chlordane. Identification of the metabolites was as follows:

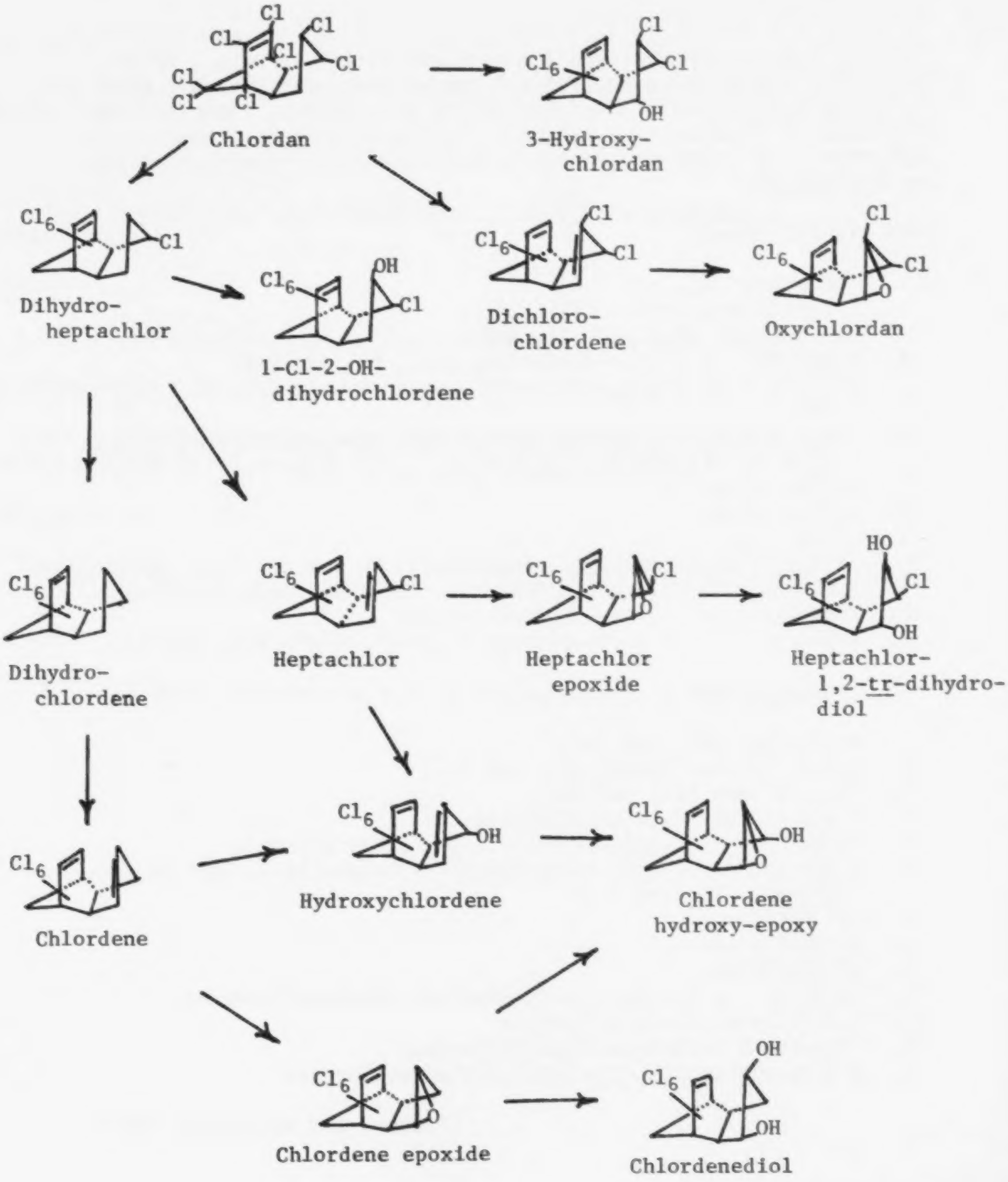
From *cis*-chlordane:

C-1. Heptachlor (GLC and TLC)
2. 1,2-dichlorochlordene (TLC only)
3. Oxychlordane (GLC, MS, IR, NMR)
4. 1-*exo*-Hydroxy-2-chlorochlordene (GLC, MS, IR, NMR)
5. 1-*exo*-Hydroxy-2-*endo*-chloro-2,3-*exo*-epoxychlordene (GLC, IR, MS, NMR
6. 1-*exo*-Hydroxy-2-*endo*-chlorodihydrochlordene (Chlordene chlorohydrin) (GLC and TLC)
7. Unidentified.
8. Unidentified.
9. Unidentified.
10. Unidentified (probably 3 compounds).
11. 1,2-Dihydroxydihydrochlordene (IR, MS, NMR)
12. Probably a trihydroxydihydrochlordene
13. β-Glucuronide of 1-*exo*-hydroxydihydrochlordene (GLC and TLC).

From *trans*-chlordane:

T-1. Heptachlor (GLC and TLC)
2. 1,2-dichlorochlordene (GLC and TLC)
3. Oxychlordane (GLC and TLC)
4. 1-*exo*-Hydroxy-2-chlorochlordene
5. 1-*exo*-Hydroxy-2-*endo*-chloro-2,3-*exo*-epoxychlordene
6. 1-*exo*-Hydroxy-2-*endo*-chlorodihydrochlordene (Chlordene chlorohydrin) (GLC and TLC)
7. Unidentified.
8. Unidentified.
9. Unidentified.
10. Unidentified (probably a monohydroxy dihydrochlordene)
11. 1,2-Dihydroxydihydrochlordene
12. Probably a trihydroxydihydrochlordene
13. β-Glucuronide of 1-*exo*-hydroxydihydrochlordene.

(Tashiro and Matsumura, 1977)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Hydroxychlordene
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Chlordene hydroxy-epoxy
Cl_6
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Chlordene epoxide
OH
Cl_6
OH
Chlordenediol

In vitro metabolism of *cis*- and *trans*-chlordane were studied with human and rat liver microsomal preparations. Metabolites identified included: 1,2-dichlorochlordene; oxychlordane; chlordene chlorohydrin; and 1,2-dihydroxychlordene. The dichlorochlordene was not observed in rat incubations with *trans*-chlordane. Four other compounds were not identified (Tashiro and Matsumura, 1978).

Studies with the metabolites gave the following results:

Starting Compound	Products
1.	11(±)
2.	3,4,5,6(±), 11(±)
3.	4,5,6(±), 11(±)
4.	5(±)
5.	---
6.	4, 11(±)
10.	---
11.	12
1-OH.[a]	13

a. 1-*exo*-hydroxydihydrochlordene

(Tashiro and Matsumura, 1977).

An *in vitro* incubation of chlordane was conducted with washed rat liver microsomes. Extracts of this incubation were analyzed with GC-MS. Differences between *cis*- and *trans*-chlordane were qualitative and quantitative. Both *cis*- and *trans*-chlordane produced dichlorochlordene, oxychlordane, 1-chloro-2-hydroxydihydrochlordene, and hydroxychlordene. In addition to these metabolites, incubations with the *cis*-analog contained dihydroheptachlor and those with the *trans*-analog contained heptachlor and hydroxychlordane (Brimfield et *al*., 1978).

Rabbits were administered *cis*- and *trans*-chlordane orally in four doses. About 77% of the *cis*-isomer and 82% of the *trans*-isomer were excreted in feces and urine. Qualitative differences were observed in metabolism of the two isomers. *Cis*-chlordane gave rise to 1-hydroxy-2-chlorochlordene, *trans*-chlordene chlorohydrin, and 1-hydroxychlordene. Metabolites produced from *trans*-chlordane were identified as 1-hydroxy-2-chlorochlordene, 1,2-dichlorochlordene, *trans*-chlordene chlorohydrin, and 3-hydroxychlordane (Balba and Saha, 1978).

Fry of fish exhibit greater hepatic mixed-function oxidase (MFO) activity than adult fish. This activity toward chlordene was exhibited by bass, bluegill, trout, oscar, peacock, Congo cichlids, and barbs. Chlordene underwent epoxidation and hydroxylation simultaneously but the epoxidation rate in each case was higher than that of hydroxylation. In mice this was reversed. It was also observed that mouse MFO activity was higher by almost 2X than that highest rate exhibited by the fish (Stanton and Khan. 1973). Female cichlids, Cichlasoma sp., produced at least six metabolites from cis-chlordane. One was identified as 1,2-dichlorochlordene (Feroz and Khan, 1977). In vivo studies with cichlids, bluegill and goldfish showed the formation of oxychlordane, chlordene chlorohydrin, and heptachlor diol from cis-chlordane in addition to dichlorochlordene and several unidentified compounds (Khan, 1978). Hepatic MFO of the aquatic frog, Xenopus laevis, caused epoxidation and hydroxylation of chlordene. However, 1-hydroxy-2,3-epoxychlordene was not observed (Doherty and Khan, 1978).

The estuarine fish, spot (Leiostomus xanthurus), was exposed to technical heptachlor for 24 days. Heptachlor, t-chlordane, cis-chlordane, and nonachlor, which were present in the technical grade heptachlor, accumulated in edible fish tissue. Heptachlor epoxide formed and was also accumulated (Schimmel et al., 1976b).

Analytical grade heptachlor was concentrated by shrimp (Penaeus duorarum) and spot fish (Leiostomus xanturus). Concentration factors were calculated to be 300-600 and 3600-10000, respectively. Heptachlor epoxide concentration factor was 200-1700 in the shrimp. When estuarine organisms were exposed to technical heptachlor, the trans-chlordane accumulation factor was 9000-16800 for Cyprinodon variegatus and 3700-14800 for spot. Concentration factors for heptachlor are summarized:

Species	Factor
Crassostrea virginica	3900-8500
Cyprinodon variegatus	7400-21300
Lagodon rhomboides	2800-7700
Leiostomus xanthurus	3000-13800
Palaemonetes vulgaris	500-700
Panaeus duorarum	200-300

(Schimmel et al., 1976a)

When exposed to chlordane, the earthworm (Lumbricus terrestris L.) excreted in excess of 95% the injected pesticide. Analyses indicated the formation of oxychlordane, chlordane chlorohydrin, dihydroxychlordane, some conjugated material, and about three unidentified compounds (Chio and Sanborn, 1976).

In a model terrestrial-aquatic ecosystem, analyses indicated the presence of 20 compounds, none identified, when ^{14}C-cis:trans (75:25) chlordane was used (Sanborn et al., 1976).

An emulsifiable concentrate of chlordane was applied at 3.4 kg Ai/ha and incorporated into sand and muck soil. Analyses indicated that 77% of the trans- and 84% of the cis-chlordane dissipated from sand and 36% and 40%, respectively, from muck. After 3 years, 89% of trans- and 84% of cis-chlordane dissipated from sand; 70% and 64%, respectively, from muck. Residues were absorbed by radishes and carrots (Harris and Sans, 1975). When alfalfa was grown in chlordane treated plots, small amounts of chlordane penetrated into the plant tissues. Photo-cis-chlordane was below the limit of sensitivity and oxychlordane was observed in second cutting only (Tafuri et al., 1977).

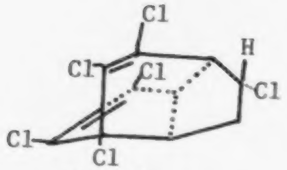
Heptachlor was incorporated into a field and its disappearance followed for more than 4.5 years. Disappearance followed first-order kinetics according to

$$\log H = 0.063 - 0.33T$$

where H = ppm and T = years. Heptachlor epoxide and hydroxychlordene were identified in the soil (Freeman et al., 1975).

A chlordene analog (I) was treated with ozone in carbon tetrachloride. Spectroscopic and structural analyses indicated structure III. Treatment of II with KI in methanol produced III. Dehydrohalogenation produced IV and V (Gab et al., 1976).

When irradiated in methanol with UV, chlordene underwent photocycloaddition and photodechlorination. Products are shown in the following table (Gab et al., 1975). (The structures shown for chlordene itself are as given but seem to be at variance with that given by other authors.)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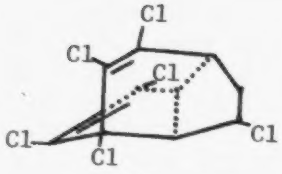
α-Chlordene
I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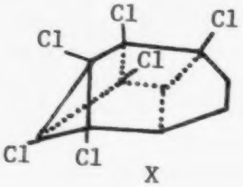
β-Chlordene
VI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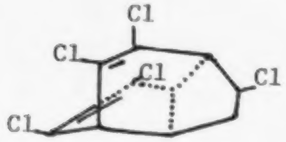
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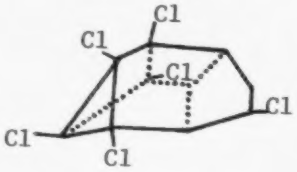
II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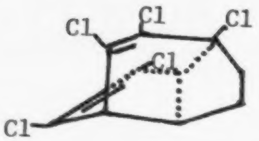
VII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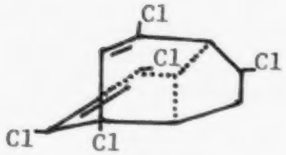
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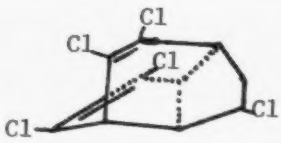
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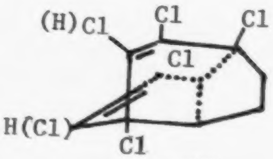
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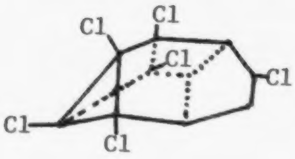
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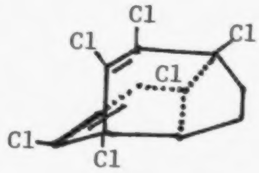
IV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γ-Chlordene
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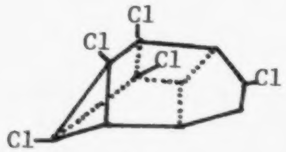
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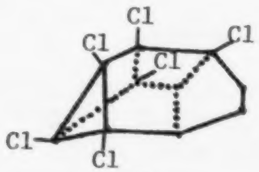
V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X

HEPTACHLOR

^{14}C-Heptachlor was administered to rats. Analyses of feces showed the presence of the following metabolites: heptachlor epoxide (13.1%), 1-*exo*-hydroxychlordene (19.5%), 1-*exo*-hydroxy-2,3-*exo*-epoxychlordene (17.5%), 1,2-dihydroxydihydrochlordene (3.5%), and 1-*exo*-hydroxy-2,3-*exo*-epoxy-3a,7a-dehydrochlordene. With *in vitro* studies with human and rat liver microsomal preparations, heptachlor epoxide, hydroxychlordene, hydroxy-epoxychlordene and the dihydroxychlordene were observed (Tashiro and Matsumura, 1978).

The estuarine fish, spot (*Leiostomus xanthurus*), was exposed to technical heptachlor for 24 days. Heptachlor, *t*-chlordane, *cis*-chlordane, and nonachlor, which were present in the technical grade heptachlor, accumulated in edible fish tissue. Heptachlor epoxide formed and was also accumulated (Schimmel et al., 1976b).

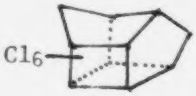
Heptachlor was applied to cabbage leaves and exposed to sunlight for 4 days. Noon temperatures were 25-28C. The cage molecule XVII was observed. When heptachlor epoxide was used, compound XVIII arose and reacted to give XIX (Parlar, 1978).

Irradiation of heptachlor produced a variety of products. Exposure of a heptachlor film to sunlight during summer months produced XXII and XXIII. At 310 nm, the dechlorinated product XXIV formed. In the presence of ceryl alcohol and acetone, the photoaddition compounds XXV-XXVIII and some partially characterized dimers XXIX-XXXII formed (Ehmann, 1976).

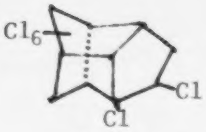
In acetone, UV irradiation of heptachlor epoxide produced the photoisomers XXXVIII and XXXIX (Knox et al., 1973).

β-Dihydroheptachlor was irradiated with a Philips HPK 125 mercury high-pressure lamp and pyrex filters in dioxane/sensitizer (30:1). Compounds XL-XLV were observed at temperatures above -70C (Parlar and Mansour, 1978).

Catalytic dechlorination of heptachlor and chlordane with nickel boride yielded a common product mixture with a common major component XLV (Dennis and Cooper, 1976).



XIV



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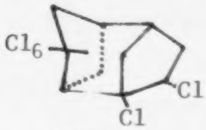

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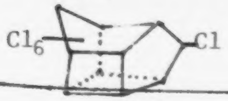

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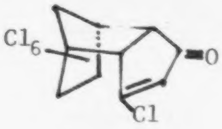

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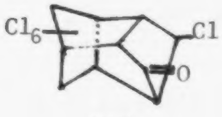

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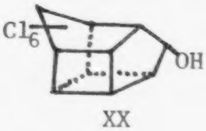
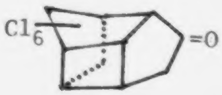
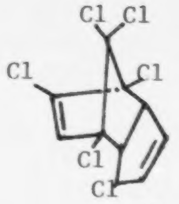


XX



XXI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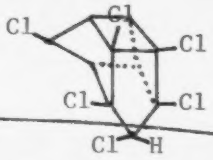
XXII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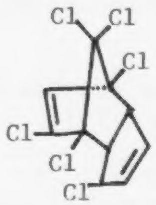
XXIII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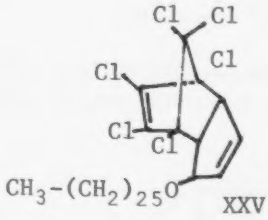
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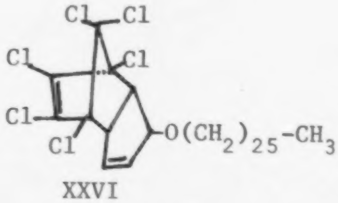
XXV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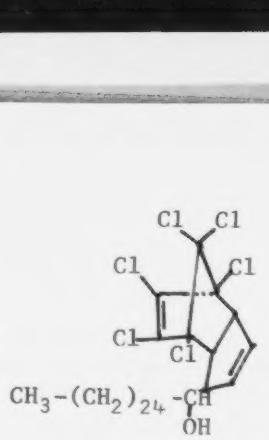
XXVI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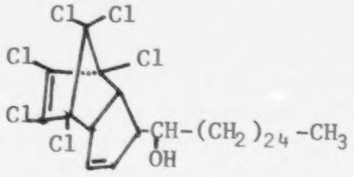
XXVII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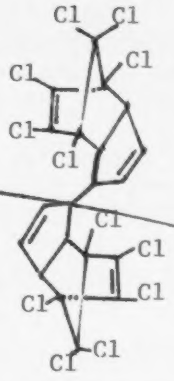
XXVIII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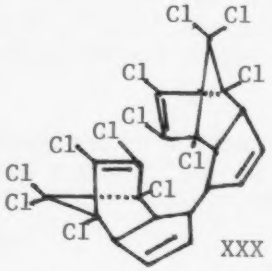
XXIX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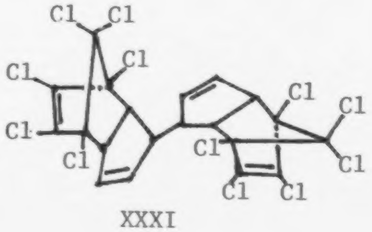
XXX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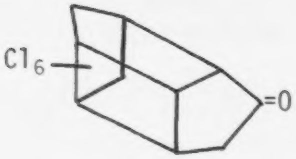
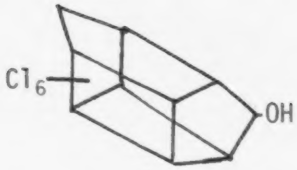
XXXI

When 1-*exo*-hydroxychlordene was irradiated with UV light (λ>290 nm) in organic solvents, on plant surfaces, or as a solid on glass, dechlorination, oxidation, and/or polymerized products were observed. Two compounds were isolated and identified by gas chromatography and NMR and mass spectroscopy (Parlar et al. 1978).





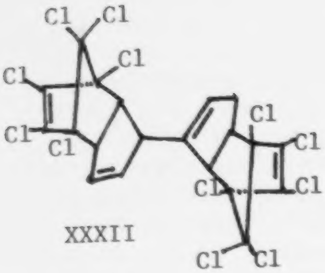
NONACHLOR

^{14}C-*Trans*-nonachlor, which comprises about 7% of technical chlordane, was administered to rats in corn oil as a single dose. Feces and urine were collected. The bulk of the radioactivity appeared in the feces and was identified as: 1,2-dihydroxydihydrochlordene (17.9%), 1-hydroxy-2-chlorochlordene (15.4%), chlordene chlorohydrin (13.5%), oxychlordane (4.1%), *trans*-chlordane (0.8%), and 1-hydroxy-2-chloro-2,3-epoxychlordene. There were two unidentified compounds and unchanged nonachlor (Tashiro and Matsumura, 1978).

In vitro studies with human and rat liver microsomal preparations showed the presence of *trans*-chlordane, oxychlordane, chlordene chlorohydrin, and 1,2-dihydroxydihydrochlordene. With human liver preparations, the level of metabolites was very low. This correlates with the finding of *trans*-nonachlor as the major chlordane residue found in human tissues (Tashiro and Matsumura, 1978).

The estuarine fish, spot (*Leiostomus xanthurus*), was exposed to technical heptachlor for 24 days. Heptachlor, *t*-chlordane, *cis*-chlordane, and nonachlor, which were present in the technical grade heptachlor, accumulated in edible fish tissue. Heptachlor epoxide formed and was also accumulated (Schimmel et al., 1976b).

UV irradiation of nonachlor in acetone produced the half-cage photoisomers believed to be XXXVI or XXXVII (Knox et al., 1973).



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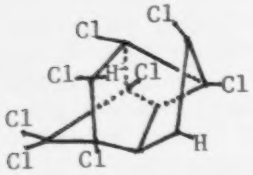

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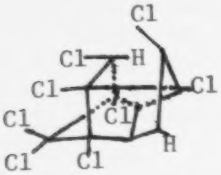

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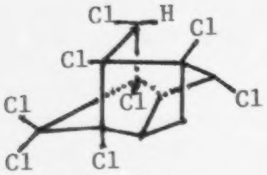
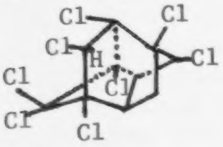
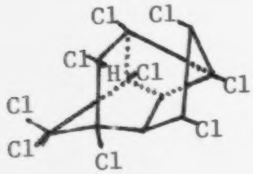


XXXVa

or



XXXVb



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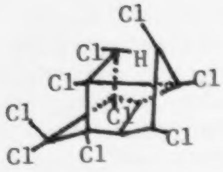

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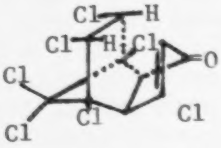

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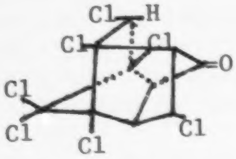

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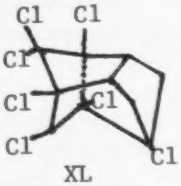
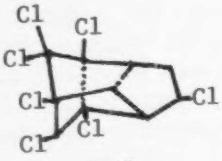
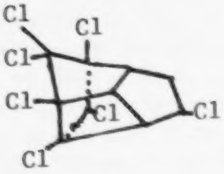


XL



XLI



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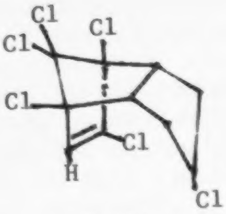

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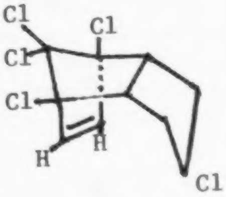


XLIV

CHLORDIMEFORM (Galecron, Fundal, Chlorphenamidine) [N-(4-Chloro-o-tolyl) N',N'-dimethylformamidine]

When ^{14}C-labeled demethylchlordimeform (II) was orally administered to rats, within 72 h 64% of label was eliminated in the feces and 35% in urine. In addition to unreacted demethylchlordimeform, 4-chloro-o-toluidine (V), 4-chloro-o-formotoluidide (IV), 5-chloroanthranilic acid (VII), and N-formyl-5-chloroanthranilic acid (VI) were identified in urine and feces. Also observed and tentatively identified was N-(4-chloro-o-tolyl)formamidine (III). Four other compounds were not identified (Benezet and Knowles, 1976). In other studies, Swiss-Webster male mice were injected intraperitoneally and male Sprague-Dawley rats were orally administered ^{14}C-chlordimeform. Elimination was very rapid. Studies were also conducted with rat liver microsomes. The same metabolites were present in each case. Only quantitative differences were observed. Compounds observed included II, III, IV, V, VI and VII as well as the three ureas X, XI and XII (Knowles and Benezet, 1977).

When applied to apples, chlordimeform disappeared rapidly from the surface of the treated apples. Sixty days after application, although less than 1% of the applied material was recovered from the apple surface, 25% was distributed within the peel and pulp. The residue was primarily unchanged chlordimeform. The major degradation product was identified as 4-chloro-o-formotoluidine (Witkonton, 1974).

About 45% of foliarly applied ^{14}C-chlordimeform was absorbed immediately. The balance volatilized within 2 h from the leaf surfaces. Labeled metabolites observed included N'-(4-chloro-o-tolyl)-N-methylformamidine (II), 4-chloro-o-formotoluidide (IV), and 4-chloro-o-toluidine (V). The remainder was unidentified but appeared to contain some conjugated material (Bull, 1973).

Two spotted spider mites were exposed to chlordimeform. Chromatographic analyses indicated the presence of metabolites II, III, IV, V, and a compound which behaved chromatographically similar to metabolite XII. When demethylchlordimeform (II) was used, in addition to unreacted II, metabolites III, IV and V were observed (Chang, 1977; Chang and Knowles, 1977). Larval instars of the cabbage looper, *Trichoplusia ni* (Hubner), were exposed to chlordimeform and the demethyl analog. Only qualitative differences were observed. Slower penetration and metabolism in the third instar than in the fifth instar was observed. Compounds II, III, IV and V were observed in both instars, as well as some unidentified material, when chlordimeform was applied. Metabolism of II showed a similar pattern. Piperonyl butoxide slowed penetration and metabolism (Crecelius and Knowles, 1976).

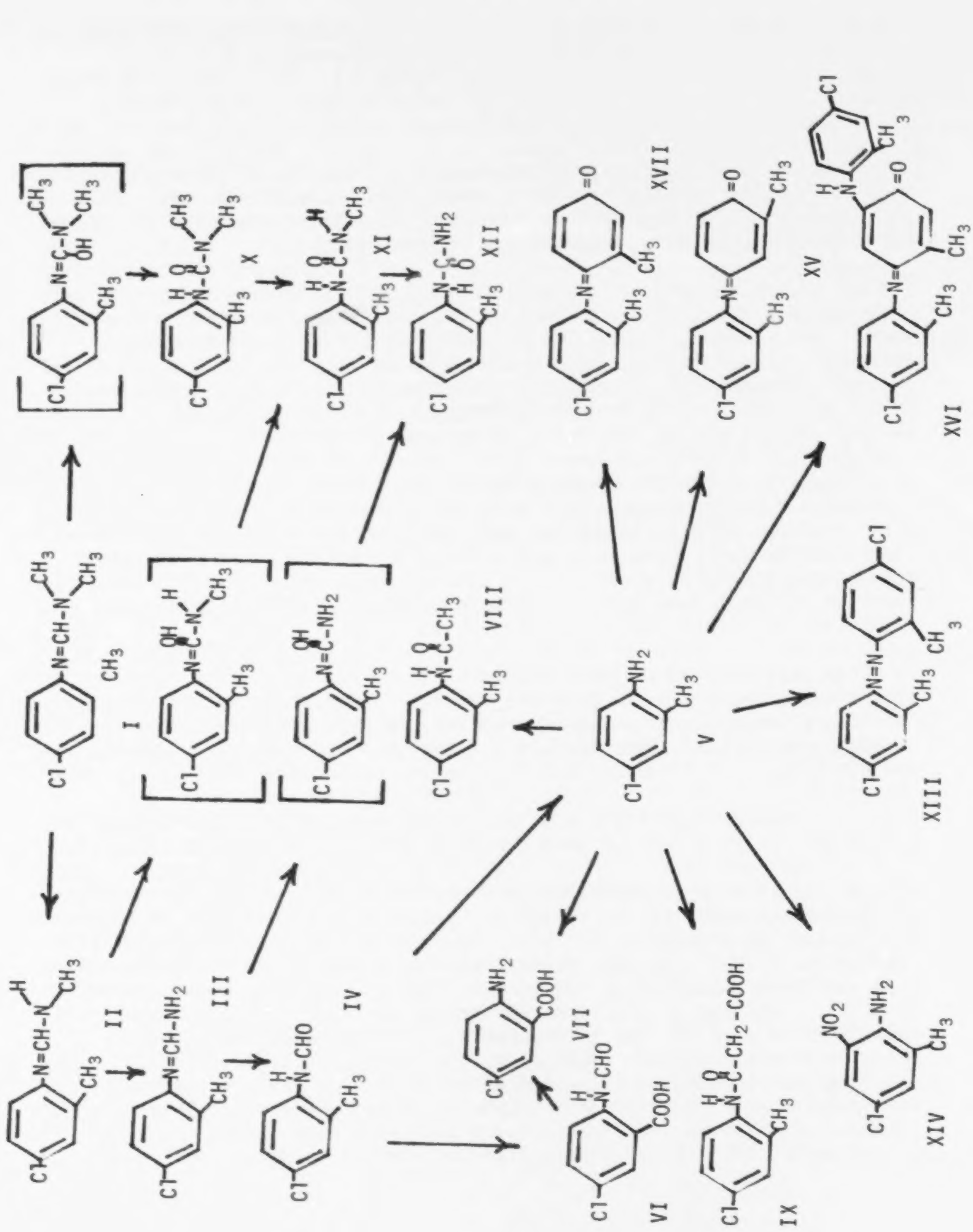
Cattle ticks (*Boophilus microplus*) absorbed chlordimeform and metabolized this material to the *N*-demethylchlordimeform (II), 4-chloro-*o*-formotoluidide (IV), and 4-chloro-*o*-toluidine (V). An unidentified polar metabolite was also formed. Piperonyl butoxide blocked the *N*-demethylation (Knowles and Schuntner, 1974).

Chlordimeform underwent rapid metabolism when injected or topically applied to houseflies. Metabolites identified included compounds II, IV, and V. *N*-Demethylation was also observed with microsomes from housefly abdomen homogenates (Knowles and Shrivastava, 1973).

[^{14}C-Tolyl]-chlordimeform was added to soil and to soil plus straw. After about 7 days, $^{14}CO_2$ evolved and continued for more than half a year. Under anaerobic conditions, very little $^{14}CO_2$ was produced. Metabolites identified included *N*-demethylchlordimeform (II), 4-chloro-*o*-formotoluidide (IV), 4-chloro-*o*-toluidine (V), and 4-chloro-*o*-acetotoluidide (VIII). Some 3-chloroanthranilic acid (VII) appeared in soil samples without straw. In soil samples with straw, formation of 4,4'-dichloro-2,2'-dimethylazobenzene (XIII) was not observed at low levels of chlordimeform but did appear after 30 days at 200 ppm chlordimeform. Four other compounds, appearing as minor compounds in soil with 2 ppm chlordimeform, were isolated from soil with 200 ppm chlordimeform and identified as the benzoquinone anils XV, XVI and XVII. Under anaerobic conditions, *N*-demethylation did not occur. Hydrolysis was the major reaction and was responsible for the formation of 4-chloro-*o*-formotoluidide (IV) (Iwan and Goller, 1974).

In other studies, one of the products observed during soil degradation of chlordimeform was 4-chloro-*o*-toluidine. Products arising from 4-chloro-*o*-toluidine were isolated from soil 90 days after incubation of soil samples with chlordimeform. These were identified through MS and syntheses as 4,4'-dichloro-2,2'-dimethyl azobenzene (XIII); 4-chloro-6-nitro-*o*-toluidine (XIV); *N*-(4-chloro-*o*-tolyl)-2-methyl-*p*-benzoquinone monoimine (XV); and 2-(4-chloro-*o*-toluidino)-*N*-(4-chloro-*o*-tolyl)-6-methyl-*p*-benzoquinone monoimine (XVI) (Iwan et al., 1976).

When soluble powder or emulsifiable concentrate formulations of chlordimeform was applied to Hagerstown silt loam soil, the residue decreased rapidly but 10% was detectable after 500 days. The material did not readily leach or accumulate in the depths of field plots. Trace amounts were observed in turnips but no accumulation occurred in carrots or potatoes. 4-Chloro-*o*-toluidine, accounting for less than 20% of the chlordimeform applied, was formed and exhibited greater persistence than the parent material. When high levels (45 lb a.i./A) of chlordimeform were applied to soil, 4,4'-dichloro-2,2'-dimethylazobenzene was isolated and identified but found not to be persistent. This compound also formed in non-autoclaved soil when high levels of chlordimeform or 4-chloro-*o*-toluidine was present. The azo derivative


I
II
III
IV
V
VI
VII
VIII
IX
X
XI
XII
XIII
XIV
XV
XVI
XVII

and 4-chloro-*o*-formotoluidine also arose from the action of sunlight on 4-chloro-*o*-toluidine. The 4,4'-dichloro-2,2'-dimethylazobenzene was absorbed by cabbage and corn and translocated to aerial parts but disappeared rapidly (Witkonton, 1974).

CHLORFENPROP-METHYL (Bidisin) [Methyl 2-chloro-3-(4-chlorophenyl) propionate]

Wild oats, *Avena sativa* L., were exposed to chlorfenprop-methyl. Hydrolysis was rapid and complete upon penetration of the leaf to give the acid (Fedtke and Schmidt, 1977).

In sandy and loamy soils, this herbicide was hydrolyzed within a few hours to the acid (CPP) which exhibited a half-life of about 4-8 days at 22 ppm but only one day at 4.4 ppm in the soil. The acid was degraded by microorganisms to 4-chlorocinnamic acid and then to 4-chlorobenzoic acid. The latter was further degraded via ring cleavage. The microorganisms have been tentatively identified as *Flavobacterium* sp. and *Brevibacterium* sp. (Kocher et al., 1976).

CHLORFENVINPHOS (Birlane) [O-[2-Chloro-1-(2,4-dichlorophenyl)vinyl] O,O-diethyl phosphate]

SD 8280 [O-[2-Chloro-1-(2,4-dichlorophenyl)vinyl] O,O-dimethyl phosphate]

On peaty soil, this pesticide degraded slowly whereas on sandy soils persistence was much shorter. When applied to the surface, the $t_{1/2}$ on peat soil was more than 150 days. On sandy loam soil, it was somewhat less than 30 days. On fine sandy soil, $t_{1/2}$ dropped to less than 4 days (Williams, 1975). In other studies, when granular formulations were applied to sandy loam soil, chlorfenvinphos $t_{1/2}$ was 10-12 weeks (Suett, 1975). Depth of incorporation of chlorfenvinphos did not affect the residue rate of decline in soil; and about 73% of a granular application, incorporated to a depth of 15 cm, dissipated within 23 weeks. Trace residues were detected in the soil as long as 4 years post application (Chisholm, 1975).

2,4-Dichlorophenacyl chloride (DCPC), a metabolite of chlorfenvinphos, was incubated with rat liver fractions and cofactors in an effort to elucidate the mechanism of formation of the metabolite 1-(2,4-dichlorophenyl)ethanol. In the presence of GSH, the reaction was spontaneous and complete within about 1 minute. With cytosol, the reaction was spontaneous also, probably binding covalently. When cytosol and GSH were present, 2,4-dichloroacetophenone formed in about 41% yield; but, if this was supplemented with NADPH and NADH, the ketone was reduced enzymatically to the alcohol. Incubation of DCPC with cytosol plus NADPH or NADH or with microsomes alone gave the chlorhydrin 2-chloro-1-(2,4-dichlorophenyl)ethanol. A small amount of 2,4-dichlorophenylethandiol was also observed in the latter incubation. Preincubation of DCPC with GSH gave the GSH conjugate which, in the presence of GSH-free cytosol, gave the ketone (Hutson et al., 1976).

The metabolism of ring-^{14}C-labeled SD 8280 was studied in rice seedlings and mature rice plants under paddy conditions in tanks. Fourteen days after foliar treatment of rice seedling with SD 8280, most of the label was present in the plant as 1-(2,4-dichlorophenyl) ethanol and this was almost completely conjugated with sugars. Small amounts of desmethyl SD 8280 and 2,4-dichlorobenzoic acid were also present. Metabolites found in rice grain and straw treated outdoors or under glasshouse conditions were the same except for 2',4'-dichloroacetophenone, which was absent in the glasshouse studies. Other metabolites observed, both free and conjugated, were desmethyl SD 8280, 1-(2,4-dichlorophenyl)ethanol, 2,4-dichlorobenzoic acid, and 2,4-dichlorophenylethan-1,2-diol. Cochromatography and radio-GLC were used to identify most metabolites. The conjugates were present primarily as glucosides. Conjugates with plant carbohydrates and other plant constituents were also indicated (Roberts and Stoydin, 1976a).

Under laboratory conditions, SD 8280 was applied to two soils from rice-growing areas in Japan and one UK soil. Degradation products were the same in each case, free and bound: 1-(2,4-dichlorophenyl) ethanol, 2,4-dichlorobenzoic acid, desmethyl SD 8280, and 2',4'-dichloroacetophenone (Roberts and Stoydin, 1976b).

CHLORINATED DIPHENYL ETHERS

CFNP [2,4-Dichloro-6-fluorophenyl 4'-nitrophenyl ether]

CHLOMETHOXYNIL (Methoxy-nitrofen, X-52) [2,4-Dichlorophenyl-3'-methoxy-4'-nitrophenyl ether]

CNP (MO) [2,4,6-Trichlorophenyl 4'-nitrophenyl ether]

NITROFEN (TOK) [2,4-Dichlorophenyl 4'-nitrophenyl ether]

When chlorinated diphenyl ethers were administered to fish, accumulation was comparable to that observed with chlorobiphenyls with a similar number of chlorines per molecule. Coefficients of accumulation from water for the 2,4,4'-, 2,3',4,4'-, and 2,2',4',5- chlorinated analogs were concentration dependent.

	96-h Exposure	
Diphenyl Ether	Concentration (µg/l)	Accumulation Coefficient
2,4,4'-Cl_3	39.3	2298
	118.0	952
2,3',4,4'-Cl_4	33.3	2720
	100.0	1025
2,2',4',5-Cl_4	31.3	1414
	94.0	588

Accumulation from food varied from 0.31 to 0.36 (Zitko and Carson, 1977).

Diphenyl ether	Solvent	Identified Photoproducts
2-Cl	Methanol	DPE; DBF
4-Cl	Methanol	DPE
2,4-Cl$_2$	Methanol	4-Cl-DPE; 2-Cl-DBF
2,4'-Cl$_2$	Methanol	4-Cl-DPE; 2-Cl-DBF
2,4'-Cl$_2$	Acetone	2-Cl-DBF
4,4'-Cl$_2$	Methanol	4-Cl-DPE; DPE
2',3,4-Cl$_3$	Acetone	1,2-Cl$_2$-DBF; 2,3-Cl$_2$-DBF
2',3,4-Cl$_3$	Methanol	2,4-Cl$_2$-DPE; 4-Cl-DPE; Cl$_2$-DPE; 1,2-Cl$_2$-DBF; 2-Cl-DBF
2,4,4'-Cl$_3$	*n*-Hexane	2,8-Cl$_2$-DBF
2,4,5-Cl$_3$	Acetone	2,3-Cl$_2$-DBF; Cl-DBF
2,4,5-Cl$_3$	Methanol	Cl$_2$-DPE; 2,4-Cl$_2$-DPE; 2,3-Cl$_2$-DBF
2,2',4,4'-Cl$_4$	*n*-Hexane	Cl$_2$-DPE; 2,8-Cl$_2$-DBF; 2,4 8-Cl$_3$-DBF
2,3',4,4'-Cl$_4$	Methanol	3,4,4'-Cl$_3$-DPE; Cl$_3$-DPE; Cl$_3$-DBF; Cl$_2$-DBF
2,4,4',5-Cl$_4$	Methanol	3,4,4'-Cl$_3$-DPE; Cl$_3$-DPE; 4,4 -Cl$_2$-DPE; 2,3,7-Cl$_3$-DBF
2,4,4',5-Cl$_4$	Acetone	2,3,8-Cl$_3$-DBF; Cl$_2$-DBF
2,4,4',6-Cl$_4$	*n*-Hexane	2,4,4'-Cl$_3$-DPE; 4,4'-Cl$_2$-DPE; 2,8-Cl$_2$-DBF; 2,4,8-Cl$_3$-DBF; 2-Cl-DBF
3,3',4,4'-Cl$_4$	Acetone	Cl$_3$-DPE; Cl$_2$-DPE
2,2',4,4',5-Cl$_5$	Acetone	Cl$_3$-DPE; 1,2,4,8-Cl$_4$-DBF; 2,3,6,8-Cl$_4$-DBF
2,2',4,4',5-Cl$_5$	Methanol	2,3',4,4'-Cl$_4$-DPE; 2,4,4',5-Cl$_4$-DPE; Cl$_3$-DPE; Cl$_4$-DBF
2,3',4,4',5-Cl$_5$	Acetone	Cl$_3$-DPE; 1,2,7,8-Cl$_4$-DBF; 2,3,7,8-Cl$_4$-DBF
2,3',4,4',5-Cl$_5$	Methanol	Cl$_4$-DPE; Cl$_3$-DPE; Cl$_4$-DBF

(Choudhry et al., 1977a and b; Norstrom et al., 1976)

CFNP [2,4-Dichloro-6-fluorophenyl 4'-nitrophenyl ether]

CFNP was added to soil samples in a flask. Flooded and upland conditions were simulated. After incubation for 2 weeks, the soils were analyzed. Degradation was much slower under upland than under flooded conditions. Degradation to the amino derivative was greater under flooded conditions. Under flooded conditions, nitrofen and CFNP were degraded more rapidly than CNP and chlomethoxynil (Niki and Kuwatsuka, 1976a).

CHLOMETHOXYNIL (Methoxy-nitrofen, X-52) [2,4-Dichlorophenyl-3'-methoxy-4'-nitrophenyl ether]

Using water and soil cultures, it was found that chlomethoxynil was rapidly absorbed and degraded by seedlings of rice and barnyard millet. The major metabolites were identified as the demethyl derivative (III), the amine (II), and the acetylated amine (V). Unidentified conjugates of the amine and demethyl metabolites were present. These were probably conjugates of saccharides, amino acids, lipids, and lignin (Niki et al., 1976).

Chlomethoxynil was added to soil samples in a flask. Flooded and upland conditions were simulated. After incubation for two weeks, the soils were analyzed. Degradation was much slower under upland than under flooded conditions. Degradation to the amino derivative was greater under flooded conditions. Under flooded conditions, nitrofen and CFNP were degraded more rapidly than CNP and chlomethoxynil (Niki and Kuwatsuka, 1976a).

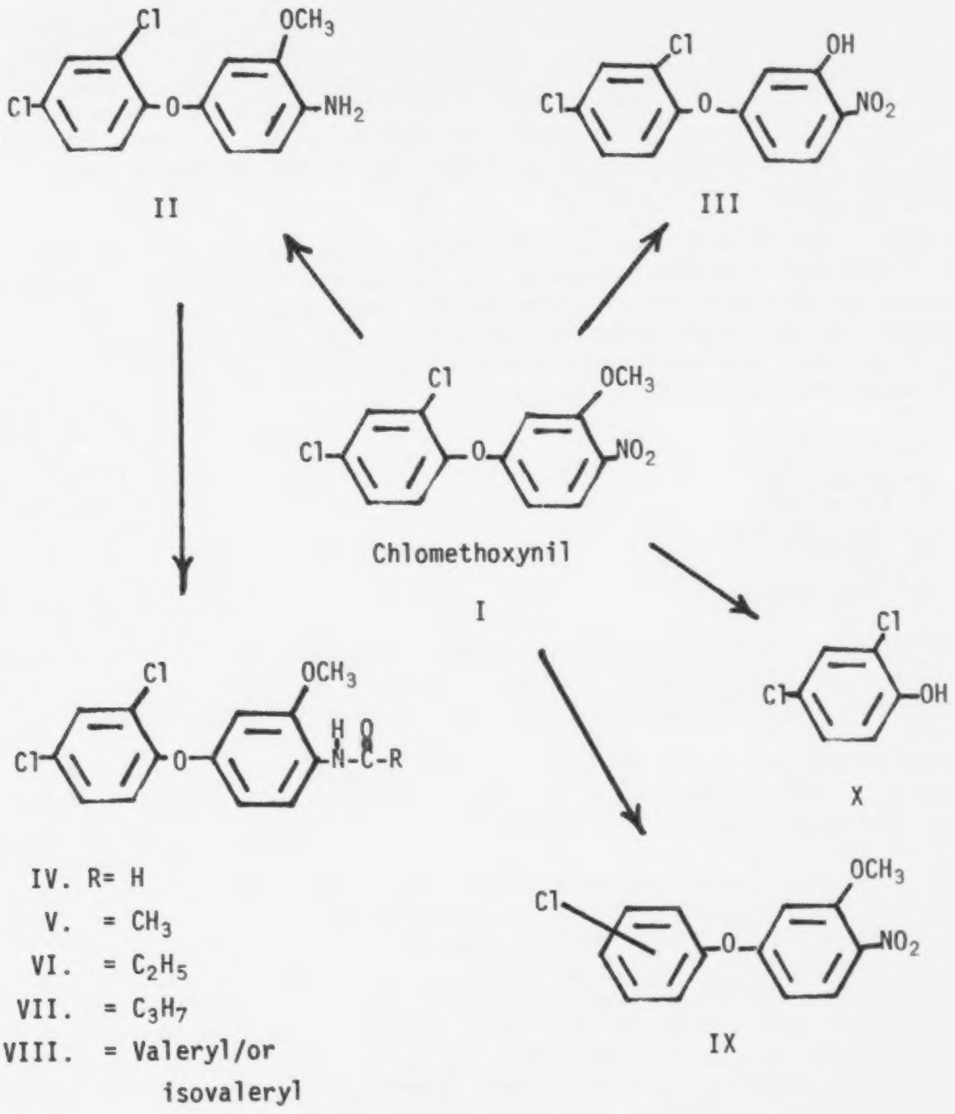
In non-sterilized soil, chlomethoxynil was rapidly degraded. Degradation also occurred in soil irradiated with ^{60}Co for 2 days and in soil treated with NaN_3 (Kuwatsuka et al., 1973).

Other studies of chlomethoxynil degradation in flooded soil showed that this material was rapidly degraded. Using TLC and GC-MS, the following degradation products have been identified:

II. 4'-amino-
III. 3'-hydroxy-
IV. 4'-formylamino-
V. 4'-acetylamino-
VI. propionylamino-
VII. butyrylamino-
VIII. valerylamino-/or isovalerylamino-
IX. a monochloro derivative
X. 2,4-dichlorophenol

The expected 3-methoxy-4-nitrophenol was not detected (Niki and Kuwatsuka, 1976b).

In a rice paddy model ecosystem, methoxy-nitrofen was degraded to a number of compounds. Of these one was identified as 2,4-dichlorophenol. The EM (ecological magnification) value in fish in this system was calculated to be 867 (Lee et al., 1976).


Cl
OCH3
NH2
O
II
OH
NO2
III
Chlomethoxynil
I
H O
N-C-R
X
IX

IV. R= H
V. = CH_3
VI. = C_2H_5
VII. = C_3H_7
VIII. = Valeryl/or isovaleryl

CNP (MO) [2,4,6-Trichlorophenyl 4'-nitrophenyl ether]

The freshwater fish topmouth gudgeon (*Pseudorasbora parva*) was exposed to 20 ppb CNP in continuous flow water. CNP concentration reached 25.3 ppm after 15 days. When placed in clean water, CNP concentration dropped to 0.115 ppm after 30 days. Analyses by TLC indicated the presence of more than 10 spots in addition to CNP. Of these only amino-CNP and *p*-nitrophenol were identified by GLC (Kanazawa and Tomizawa, 1978).

CNP was added to soil samples in a flask. Flooded and upland conditions were simulated. After incubation for two weeks, the soils were analyzed. Degradation was much slower under upland than under flooded conditions. Degradation to the amino derivative was greater under flooded conditions. Microorganisms identified as capable of degrading CNP to its amino derivative included the following:

- *P. fluorescens*
- *P. myxogenes*
- *P. aeruginosa*
- *P. azotoformans*
- *B. subtilis*
- *B. megatherium*

Under flooded conditions, nitrofen and CFNP were degraded more rapidly than CNP and chlomethoxynil. Several soil microorganisms converted CNP to its acylamino derivatives (Niki and Kuwatsuka, 1976a and b).

In non-sterilized soil, CNP was rapidly degraded. Degradation also occurred in soil irradiated with ^{60}Co for 2 days and in soil treated with NaN_3 (Kuwatsuka et al., 1973).

Two bacteria, a fungus and an actinomycete capable of degrading CNP were isolated from soil. Using these organisms, ^{14}C-CNP was incubated in culture media. $^{14}CO_2$ appeared after a 10 to 15 day lag period. Metabolites identified included CNP-NH_2, CNP-NH-$COCH_3$, *p*-nitrophenol, *p*-aminophenol, CNP-NH-CH_3, *p*-formylaminophenol. CNP-NH-$COCH_3$ was the main metabolite produced by the fungus and bacteria; CNP-NH-CH_3 and *p*-nitrophenol, by the actinomycete. In soil, under flooded conditions, CNP-NH_2, CNP-NH-$COCH_3$, *p*-nitrophenol, *p*-aminophenol, and dechlorinated derivatives were produced. The main mechanism of nitro reduction in flooded soils was apparently chemical reduction by ferrous ion. This was produced from Fe^{+++} by soil microbes. ^{14}C-CNP-NH_2 was strongly adsorbed on soil particles and degraded to give $^{14}CO_2$ (Kuwatsuka et al., 1978).

^{14}C-CNP was rapidly absorbed through rice plant roots. CNP was not metabolized to a great extent. When ^{14}C-CNP-NH_2 was used, absorption and metabolism was rapid. In the rice plant, of three metabolites observed, two were identified as 2,4,6-trichlorophenyl 4'-formylaminophenyl ether and 2,4,6-trichlorophenyl 4'-hydroxyphenyl ether. CNP-NH_2 glucoside was detected also (Shimotori and Kuwatsuka, 1978).

NITROFEN (TOK) [2,4-Dichlorophenyl 4'-nitrophenyl ether]

^{14}C-Nitrofen was administered orally to sheep. Analyses indicated that most of the dose (76.2%) was excreted in slightly over 4 days. Radiocarbon levels were highest in fat but appeared in other tissues, organs and glands. The following products of metabolism were identified:

2,4-dichlorophenyl 4-aminophenyl ether
2,4-dichloro-5-hydroxyphenyl 4-nitrophenyl ether
2,4-dichlorophenol
2-chlorophenyl 4-nitrophenyl ether
4,4'-bis(2,4-dichlorophenoxy)azobenzene

Studies indicated that glucoside, sulfate and glycine conjugates were also present (Hunt et al., 1977). Other studies have indicated annual reduction of the nitro group to the amine with subsequent acetylation (Adler et al., 1971, unpublished, from Wargo et al., 1975).

^{14}C-Ring-labeled nitrofen was applied as a preemergent herbicide in rice and wheat plots. A large portion of the activity, regardless of which ring was labeled, was found in the starch from the plants. This was verified by hydrolyses of the starch to glucose and derivatization to the osazone with phenylhydrazine (Wargo et al., 1975). Further analyses indicated that very little of the radioactivity was found in the rice and wheat straw (Honeycutt and Adler, 1975).

In a rice paddy model ecosystem, the 2,4-dichlorophenol was observed. The EM (ecological magnification) value for nitrofen was calculated to be 1546 in Gambusia vs. water (Lee et al., 1976).

Nitrofen was added to soil samples in a flask. Flooded and upland conditions were simulated. After incubation for two weeks, the soils were analyzed. Degradation was much slower under upland than under flooded conditions. Degradation to the amino derivative was greater under flooded conditions. Under flooded conditions, nitrofen and CFNP were degraded more rapidly than CNP and chlomethoxynil (Niki and Kuwatsuka, 1976a).

CHLOROPICRIN (Telone) [Trichloronitromethane]

In the presence of 1 ppm ozone, photolysis of telone produced 3-chloropropionyl chloride (Moilanen et al., 1977).

In a vapor phase photoreactor, when chloropicrin was subjected to sunlight wavelengths, photolysis was rapid and phosgene and nitrosyl chloride were formed (Moilanen et al., 1976).

Vapor phase photodecomposition of chloropicrin produced phosgene and nitrosyl chloride. The latter decomposed to nitric oxide and chlorine. Nitric oxide, in turn, gave rise to some nitrogen dioxide and dinitrogen tetroxide (Moilanen et al., 1978).

CHLORPROPHAM (CIPC, 3-Chloroisopropyl carbanilate) [Isopropyl *N*-(3-chlorophenyl)carbamate]

PROPHAM (IPC, Isopropyl carbanilate) [Isopropyl *N*-phenylcarbamate]

When plants were exposed to chlorpropham, phenolic metabolites identified after TLC and HPLC included the 3-chloro-4-hydroxy- and 5-chloro-2-hydroxy- analogs of chlorpropham. In the susceptible oat (*Avena sativa* L.), mass spectral data indicated the presence of *S*-cysteinyl 4-hydroxychlorpropham (Still and Rusness, 1977). In the presence of soluble enzyme systems from etiolated shoots of oat seedlings, the *S*-cysteinyl and glutathione conjugates were also formed (Rusness and Still, 1977a). The site of thioether conjugation appeared to be the *ortho* position (Rusness and Still, 1977b).

Soybean shoots were exposed to CIPC for 16 days and then processed. In addition to the 5-Cl-2-HO- and 3-Cl-4-HO CIPC analogs, a third hydroxylated metabolite was observed and identified, after synthesis, as 1-hydroxy-2-propyl *N*-(3-chlorophenyl)carbamate (Wiedmann et al., 1976).

Wheat, sugarbeet, and alfalfa were treated with propham. Three polar metabolites were isolated from wheat and alfalfa extracts and one from sugarbeet extracts. After hydrolysis, the aglycone of two metabolites from wheat was identified as isopropyl 4-hydroxycarbanilate. The aglycone of the third wheat metabolite was identified as isopropyl 2-hydroxycarbanilate. The aglycone of all of the alfalfa and sugarbeet polar metabolites was identified as isopropyl 4-hydroxycarbanilate (Burt, 1977; Burt and Corbin, 1978).

Alfalfa was harvested and freeze dried after being root-treated for 7 days with ^{14}C-phenyl-labeled propham. Rats and sheep were then orally administered alfalfa roots or shoots containing ^{14}C. When the root was given, 84-89% of the ^{14}C was excreted in feces within 96 h. When the shoot was fed, 53-55% of the ^{14}C appeared in urine and 32-43% in feces. The major metabolite in urine of sheep given alfalfa shoots was identified as the sulfate of 4-HO-propham. The glucuronide was also present. Four other metabolites were not identified. When fed the alfalfa roots, eight metabolites were observed. Four were not identified. The other four were identified as conjugates of glycosides of 2- and 4-HO-propham and 4-HO-aniline. Some sulfate esters were probably present also. Analyses of rat urine gave similar results. In addition to six unidentified metabolites in urine of rats fed alfalfa roots and shoots, conjugated forms of 4-HO- and 2-HO-propham and 4-HO-aniline were tentatively identified (Paulson et al., 1975).

Alfalfa root, treated for 7 days with ^{14}C-phenyl-propham, was analyzed after 7 days. NMR, IR, and MS were used to identify the metabolites as glycosides of 2-hydroxy- and 4-hydroxy-propham (Still and Mansager

1975). In other studies, polar metabolites were extracted from propham-treated alfalfa and identified as conjugates of 2-hydroxy-, 4-hydroxy-propham and 1-hydroxypropyl 2-(N-phenyl)carbamate. A fourth aglycone was not identified. Enzyme studies indicated that the conjugates were present, at least in part as O-glycosides (Zurqiyah et al., 1976).

Metabolism of chlorpropham by alfalfa gave the corresponding 2-hydroxy- and 4-hydroxy-chlorpropham (Still and Mansager, 1975).

A humic polymer was produced by *H. toruloidea* grown on ring-^{14}C chlorpropham. About 4% of the label was released as $^{14}CO_2$ after 12 weeks of soil incubation (Wolf and Martin, 1976).

Hydrolysis of CIPC and IPC by microorganisms is shown in the following table.

	k	
	CIPC	IPC
Ps. striata	1×10^{-1}	9×10^{-2}
A. fumigatus	2.5×10^{-4}	1.5×10^{-4}

(Wolfe et al., 1978)

In natural surface waters, pH values would tend to maintain the stability of CIPC in the aquatic environment (El-Dib and Aly, 1976a). The mixed microflora of the Nile R. and sewage did not degrade IPC or CIPC. Addition of *Bacillus cereus* to the aqueous solutions did degrade IPC but not CIPC (El-Dib and Aly, 1976c). On bentonite clays, CIPC and IPC adsorption conformed to Freundlich's equation. In polluted water, removal of these compounds required a considerable amount of bentonite (El-Dib and Aly, 1976b).

Photolysis of aqueous CIPC at 25C produced the 3-hydroxy IPC with a half-life of 130 h. Simulated noonday sunlight was used. When performed in 2% aqueous acetone, photolysis yielded a second compound identified as 2-isopropoxycarbonylamino-1,4-benzoquinone (Guzik, 1978).

CHLOROTHALONIL (Daconil 2787, Exotherm, Termil, Bravo) [2,4,5,6-Tetrachloroisophthalonitrile]

When chlorothalonil was applied to apple foliage and fruit, there was no evidence of chemical breakdown (Gilbert, 1976).

At pH 7 and lower, there was no observed hydrolysis of chlorothalonil. At alkaline pH, this was hydrolyzed to 4-hydroxy-2,5,6-trichloroisophthalonitrile and 3-cyano-2,4,5,6-tetrachlorobenzamide. The reaction followed first-order kinetics (Szalkowski and Stallard, 1977).

Soil microorganisms converted daconil into 4-hydroxy-2,5,6-trichloroisophthalonitrile. This was irradiated in water, through a pyrex filter with a 450-W mercury vapor lamp. Chromatography, elemental analysis, MS and NMR were used to identify the photolytic product as 2,5-dichloro-4,6-dihydroxyisophthalonitrile (Binkley et al., 1977a and b).

Photolysis of chlorothalonil in methanol produced compounds identified by MS as II, III and IV (Binkley et al., 1977a and b). In benzene, the photolytic product was identified by MS and CMR spectra as 2,4-dicyano-3,5,6-trichlorobiphenyl. Photolysis also occurred in toluene, *o*-xylene, and mesitylene but no products were identified (Kawamura *et al.*, 1978; Loeffler, 1978).

CHLORTHIAMID (Prefix, WL 5792) [2,6-Dichlorothiobenzamide]

Chlorthiamid was rapidly converted to dichlobenil in soil. Addition of charcoal to soil decreased the rate of chlorthiamid-dichlobenil disappearance significantly (Moyer, 1973).

CHLORPYRIFOS (Dursban, Dowco 179) [*O*.*O*-Diethyl *O*-(3,5,6-trichloro-2-pyridyl)phosphorothioate]

CHLORPYRIFOS-METHYL (Dowco 214, OMS 1155, ENT 27520, Reldan) [*O*,*O*-Dimethyl *O*-(3,5,6-trichloro-2-pyridyl)phosphorothioate]

After a lethal amount of chlorpyrifos was ingested by a human, a metabolite was isolated from liver tissue and identified as an analog of chlorpyrifos with one chlorine replaced by a CH_3S-group in the 3 or 5 position (Lores et al., 1977 and 1978).

Sheep and rats were administered single oral doses of chlorpyrifos-methyl. Urine contained three major metabolites identified as 3,5,6-trichloro-2-pyridinol (IV) and its glucuronide (V), and *O*-methyl *O*-(3,5,6-trichloro-2-pyridyl)phosphorothioate (II). Compounds II and IV were also observed in sheep feces. When sheep were orally administered compound IV, the glucuronide (V) was excreted in urine (Bakke and Price, 1976).

Metabolism of chlorpyrifos by rats gave six metabolites. Three were identified as 3,5,6-trichloro-2-pyridinol and its glucuronide and another glycoside of 3,5,6-trichloro-2-pyridinol (Bakke et al., 1976b).

In other studies, meat fat analyses indicated the presence of a residue not previously observed. GC-MS was used to identify the compound as *O*,*O*-diethyl *O*-(3,6-dichloro-2-pyridyl)phosphorothioate (Luke and Dahl, 1976).

Analysis of tissues of cattle fed chlorpyrifos showed the presence of unchanged pyrifos and 3,5,6-trichloro-2-pyridinol (Dishburger et al., 1977). Milk of cows fed chlorpyrifos contained chlorpyrifos and its oxygen analog and 3,5,6-trichloro-2-pyridinol (McKellar et al., 1976).

Chlorpyrifosmethyl was applied to bermudagrass [*Cynodon dactylon* (L.) Pers.] and corn. Analyses indicated the presence only of 3,5,6-trichloro-2-pyridinol in addition to unchanged chlorpyrifosmethyl (Leuck et al., 1975).

When chlorpyrifos and the methyl analog were applied to larvae of tobacco budworms (*Heliothis virescens* F.), the principal metabolite of both S and R strains was identified as 3,5,6-trichloro-2-pyridinol. The de-methyl, but not de-ethyl, metabolite was also observed. With larval microsomal preparations, metabolism of the methyl and ethyl analogs was substantially increased by inclusion of NADPH. The addition of GSH doubled *O*-demethylation (Whitten and Bull, 1974).

After topical treatment of the Eastern subterranean termite with ^{14}C-chlorpyrifos, analyses indicated the formation of the oxygen analog, the trichloropyridinol, and six unknowns. One of the latter was tentatively identified as the 3-dechlorinated analog of chloropyrifos (Hutacharern, 1975; Hutacharern and Knowles, 1975).

The hydrolysis of chlorpyrifos in aqueous media was first order in the range of $3x10^{-9}$ to $3x10^{-7}$ M. At 25C and pH 8.1, the $t_{1/2}$ = 22.8 days; at pH 6.9, 35.3 days; and at pH 4.7, 62.7 days. Products of hydrolysis that were identified were 3,5,6-trichloro-2-pyridinol, and mono- and di-desethyl analogs of chlorpyrifos. In the case of chlorpyrifos-methyl, the $t_{1/2}$ at 25C was 12.7 days at pH 7.8; 17.4 days at pH 6.7; and 22.8 days at pH 4.2. Hydrolysis products were similar with methyl analogs replacing the ethyl compounds (Meikle and Youngson, 1978).

CILIATINE [2-Aminoethylphosphonic acid]

P-Ciliatine in a bound form in a tetrahymena acetone powder was administered orally to rats. Urine and feces was collected and analyzed. About 15% of the dose was excreted within 3 days in urine and 25% in feces. In the liver, radioactivity was found in the phospholipids, acid-soluble phosphorus, nucleic acid-P, and protein-P fractions (Tamari et al., 1975). Almost all radioactivity in the liver lipid was present in the phospholipid fraction as phosphonocephalin (90%) and phosphonolecithin (Hasegawa et al., 1975). In bovine liver, ciliatine was distributed in phosphatidylethanolamine, phosphatidyl choline, phospatidyl inositol and phosphatidyl serine (Hasegawa et al., 1976). In studies with chickens, incorporation of ciliatine into tissues was observed also (Tamari et al., 1976a).

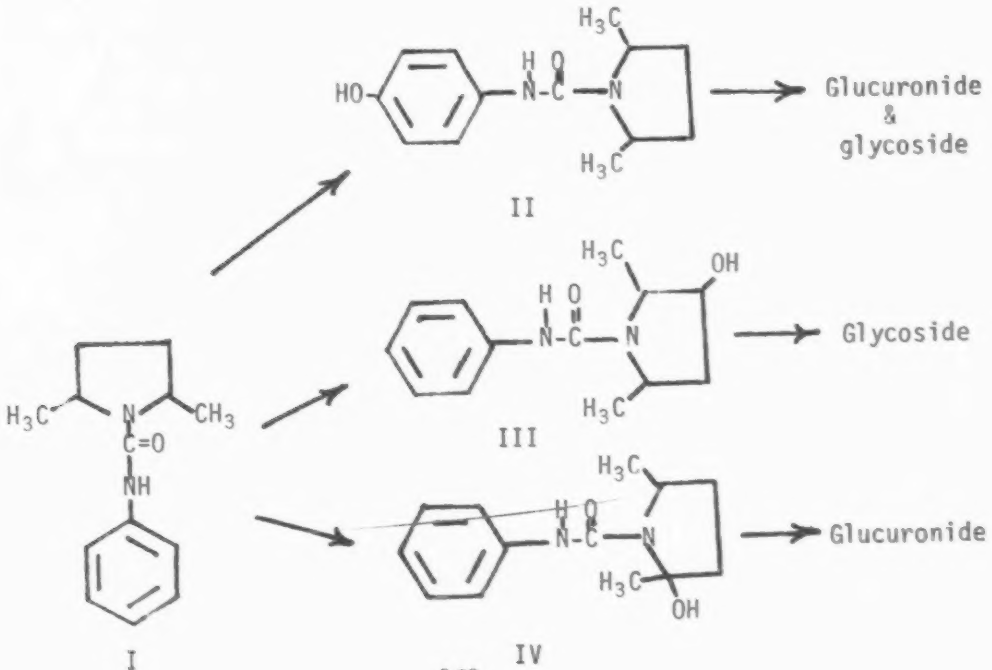
When P-ciliatine was administered intraperitoneally to Wistar rats, P-ciliatine was incorporated into nearly all tissues. A small portion of the ciliatine was decomposed prior to incorporation of the P. When administered orally, ciliatine was accumulated to a large extent in liver and other tissues (Hasegawa et al., 1973).

CISANILIDE (*cis*-2,5-Dimethylpyrrolidine-1-carboxanilide]

Cisanilide was administered to rats. Analysis of urine showed the presence of the 4'-hydroxycisanilide analog (II) as the major metabolite. In mice, the glucuronide of II was present in urine but the free phenol was not found. Aniline and 4-aminophenol were present in urine of rats, rabbits, guinea-pigs and mice given cisanilide. All species also produced II-glucuronides. Sulfate conjugate of II was found in all species except in mice (Mitchell and Waring, 1978).

In vitro metabolism of cisanilide was investigated with ^{14}C-phenyl and 2,5-pyrrolidine-^{14}C cisanilide and rat liver microsomal preparations. The primary metabolites were identified as the 2-hydroxycisanilide (IV) and the 4'-hydroxycisanilide (II). A third metabolite, not fully identified, appeared to be the 2,4'-dihydroxy analog. Hydrolysis studies with β-glucuronidase indicated that about half of the metabolites were present as their glucuronides. The microsomal activity was associated with an MFO requiring O_2 and NADPH (Frear and Swanson, 1975b and 1976).

Excised cotton (*Gossypium hirsutum* L.) and carrot (*Daucus carota* L.) leaves were exposed to cisanilide. Appreciable hydrolysis of the molecule did not occur in 6 days. In carrots, two glycosides comprising 50% of total ^{14}C were the major metabolites after 6 days. With IR and FT-NMR, two metabolites were identified as glycosides of 4'-hydroxycisanilide and 3-hydroxycisanilide. Metabolism by cotton leaves was similar (Frear and Swanson, 1975a; Frear et al., 1975).



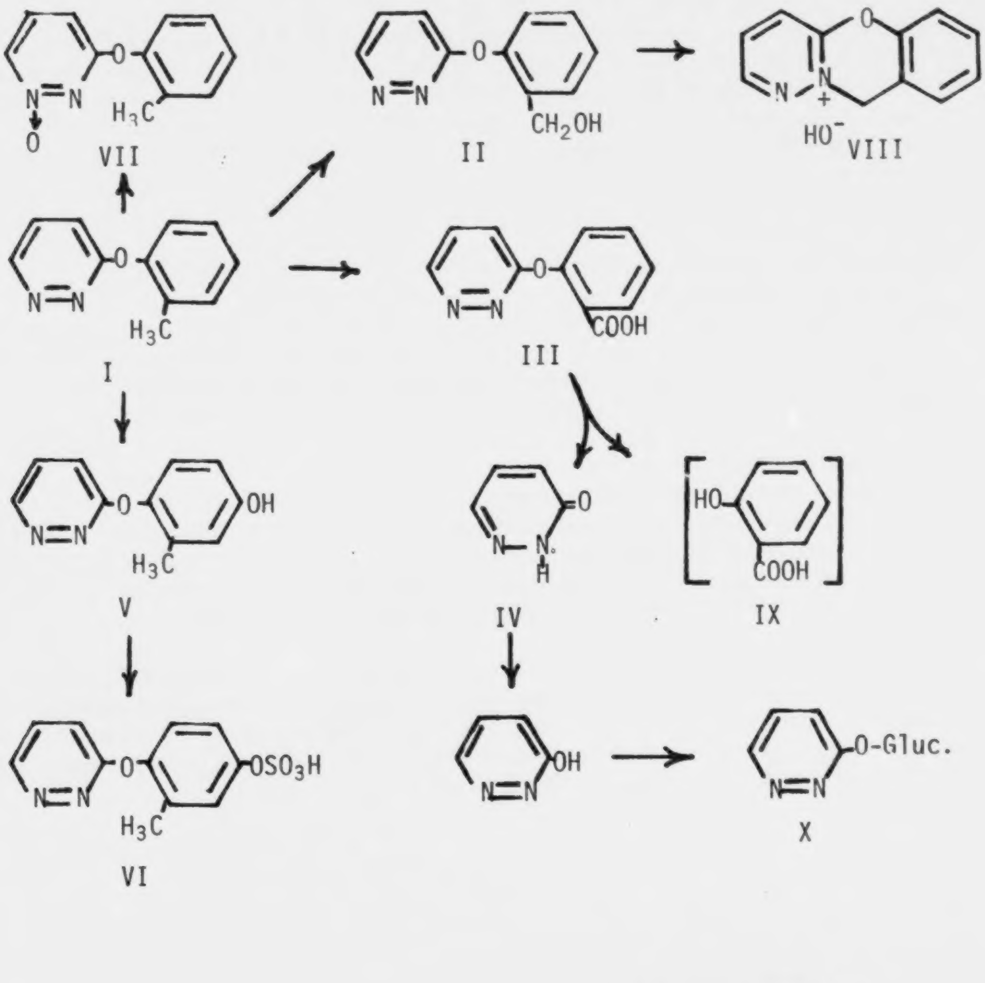
COUMARIN [1,2-Benzopyrone]

When coumarin was injected into rats, about 31% of the dose was excreted via feces and 47% via urine within 100 h. About 7% remained in the tissues. The highest tissue concentrations were in kidney and liver (Piller, 1977).

CREDAZINE (H-722) [3-(2'-Methylphenoxy)pyridazine]

Credazine was administered to male Wistar rats as a single oral dose at the rate of 10 and 100 mg/kg. Urinary metabolites were identified as the 3-(2'-hydroxymethylphenoxy)pyridazine (II), 3-phenoxypridazin-2'-yl carboxylic acid (III), 3(2H)-pyridazinone (IV), and 3-(2'-methyl-4'-hydroxyphenoxy)pyridazine sulfate (VI). Another minor metabolite was identified as 3-(2'-methylphenoxy)pyridazine-1-oxide (VII). Compounds II and III were labile and isomerized to VIII and IV + IX, respectively (Nakagawa and Ando, 1977).

Barley (susceptible) and tomato (tolerant) plants were exposed to [6-^{3}H]-credazine. Three metabolites were identified as compounds IV, VII, and the conjugate X (Nakagawa et al., 1971).



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CREMART [*O*-Ethyl *O*-(3-methyl-6-nitrophenyl) *N*-*sec*-butylphosphoramidothioate]

Cremart, ^{3}H-phenyl-labeled, was orally administered to rats at the rate of 70 mg/kg. Excretion of this compound was rapid and primarily via urine. Within 48 h after administration, 75.8% (female) to 83.1% (male) of the cremart was excreted via urine and 24.2% (female) to 16.9% (male) was excreted in the feces. Analyses of tissues 30 minutes after i.v. injection showed that the metabolites were present in highest concentration in the liver and kidneys.

	Tissue Content (ppm)				
Compounds Found	Blood	Brain	Liver	Lung	Kidney
Cremart	<1.0	2.0	<1.0	3.3	4.0
Cremart-oxon	<0.1	<0.1	ca 0.1	<1.0	<0.1
3-methyl-6-nitrophenol	<0.1	<0.1	<1.0	<1.0	<1.0
3-hydroxymethyl-6-nitrophenol	<0.1	<0.1	<1.0	<0.1	<1.0
3-carboxy-6-nitrophenol	2.5	2.6	12.8	3.3	21.9
Unknown I	---	---	<1.0	---	---
Unknown II	---	---	1.2	---	---

Analyses of urine showed that, in addition to those metabolites in the foregoing table, the following compounds were also present.

aminocremart
6-amino-3-carboxy derivative
O-ethyl *O*-(3-methyl-6-nitrophenyl)phosphorothioate
3-methyl-6-nitrophenyl sulfate
3-hydroxymethyl-6-nitrophenyl sulfate and β-glucuronide
3-carboxy-6-nitrophenyl-β-glucuronide

When plants were exposed to ^{3}H-cremart dissolved in nutrient solution, this herbicide was readily taken up. Metabolites observed and identified in bean, rice, and carrot plants included the following: cremart; 3-methyl-6-nitrophenol; 3-methyl-6-nitrophenyl-β-glucoside; cremart oxon; and 3-hydroxymethyl cremart (Mihara et al., 1976).

CRONETON (Bay Hox 1901) [2-Ethylthiomethylphenyl N-methylcarbamate]

^{14}C-Croneton was administered as a single oral dose to albino rats. When ^{14}C-carbonyl-labeled croneton was given, within 8 h about 47% of the dose was eliminated as $^{14}CO_2$; and about 41% in urine and 7% in feces within 3 days. After administration of ^{14}C-ring-labeled-croneton, about 96% of the dose was found in urine and 2% in feces. Analyses of urine indicated the presence of the following compounds in addition to unchanged croneton:

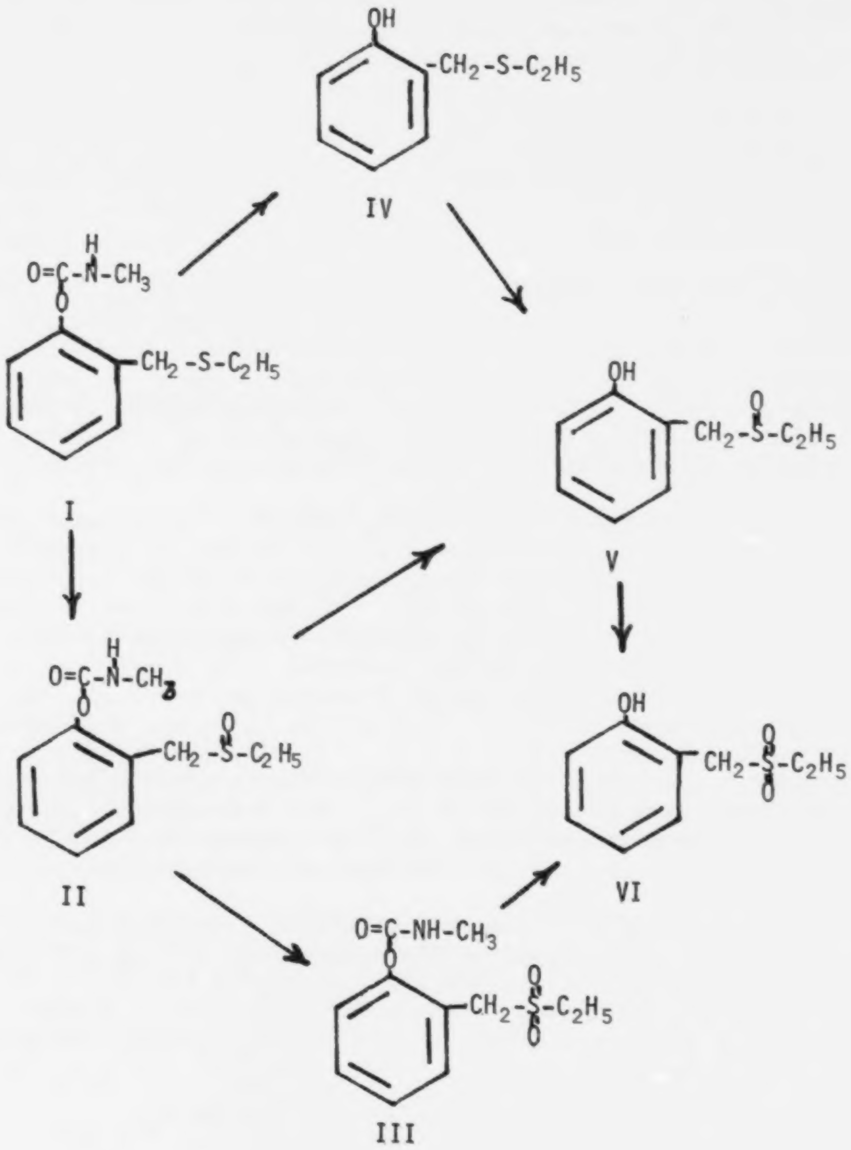
croneton sulfoxide
croneton sulfone
2-ethylthiomethylphenol
sulfoxide phenol
sulfone phenol

When croneton sulfoxide or sulfone was administered, in addition to the sulfoxide/or sulfone, the sulfone phenol was found (Nye et al., 1976). In rats and mice, hydrolysis of the ester destroyed the toxicity of croneton, the sulfoxide and sulfone. In lactating cows, in pigs, and in laying hens, the predominant metabolic pathways included oxidation of the sulfur, hydrolysis of the ester, and conjugation of phenolic metabolites (Dorough and Nye, 1976).

At planting of beans and potatoes, carbonyl-^{14}C-croneton was applied in granular form. Subsequent analyses showed the presence of the sulfoxide and sulfone in the extractable fraction. Confirmation of structure was by IR, NMR and MS. ^{14}C was also found in the potato starch and cellulose and incorporated into glucose (Drager, 1978).

Bean plants metabolized applied croneton and produced some conjugated water-soluble metabolites. Most of the plant residues were conjugates of croneton phenol sulfoxide and sulfone. Some carbamates were also present. When these conjugates were fed to rats, carbamates were hydrolyzed as were the glucosides. The free hydroxy groups formed by glucoside hydrolysis were again conjugated as glucuronides and other possible derivatives (Marshall and Dorough, 1977).

In soil, carbonyl-^{14}C-croneton was rapidly oxidized to the sulfoxide and sulfone. Hydrolysis to CO_2 occurred in soil as well as in water (Drager, 1978).

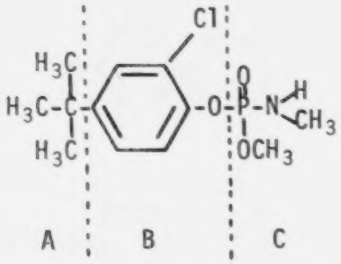

OH
-CH2-S-C2H5
IV
H
O=C-N-CH3
O
CH2-S-C2H5
I
OH
O
CH2-S-C2H5
V
H
O=C-N-CH3
O
O
CH2-S-C2H5
II
OH
O
CH2-S-C2H5
O
VI
O=C-NH-CH3
O
O
CH2-S-C2H5
O
III

CRUFOMATE [*O*-(4-*tert*-Butyl-2-chlorophenyl) *O*-methyl *N*-methylphosphoramidate]

Male rats were administered ^{14}C-labeled crufomate by stomach tube. Urine and feces were collected and analyzed. Using TLC, derivatization and GLC-MS, 15 metabolites were identified in the excreta as compounds II, III, V to XIV, XVI, XVII, XVIII and XXII (Bakke and Price, 1977).

When everted sacs of rat small intestine were incubated with crufomate, six metabolites were formed in sufficient amounts to allow identification. These were identified as compounds III, V, VI, VIII, X and XXII (Pekas et al., 1977).

Sheep were dosed orally with ^{14}C-crufomate and urine, feces and plasma were collected and analyzed. A total of 24 metabolites were isolated and identified by syntheses and MS. Seventeen of these were nonconjugated. The remaining seven were glucuronide conjugates. These have been arranged in a suggested pathway (Bakke et al., 1976a, b and c).



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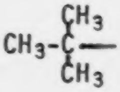
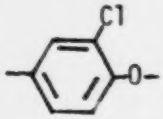
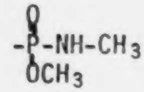
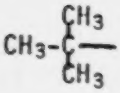
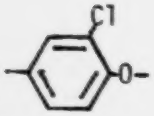
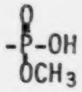
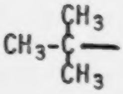
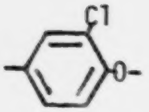
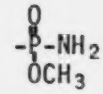
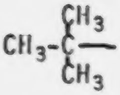
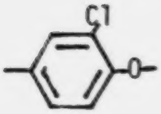
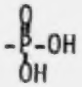
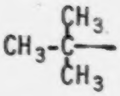
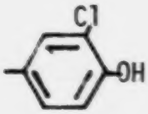
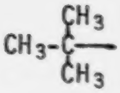
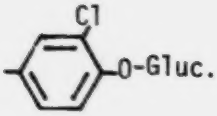
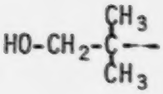
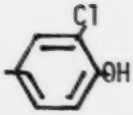
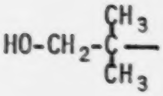
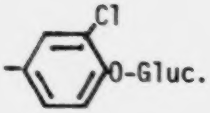
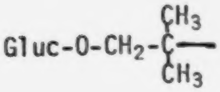
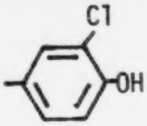
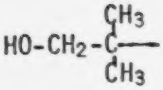
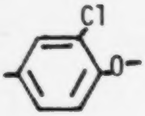
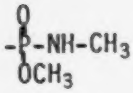
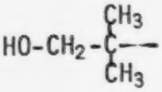
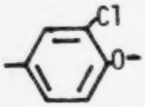
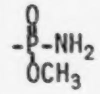
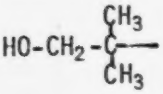
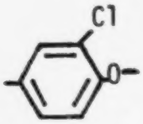
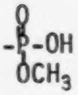
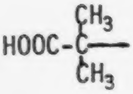
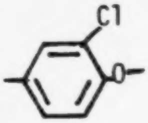
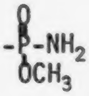
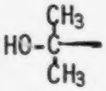
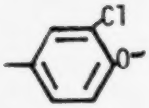
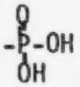
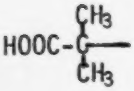
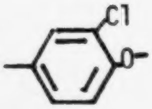
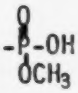
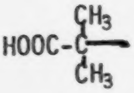
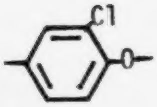
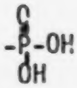
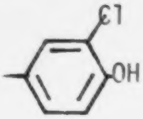
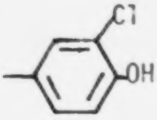
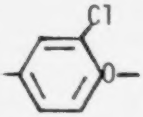
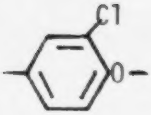
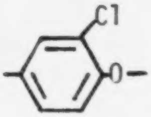
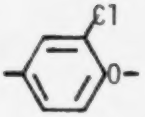
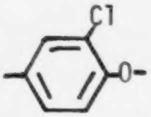
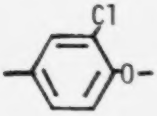
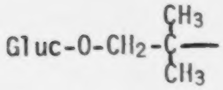
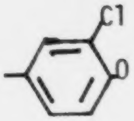
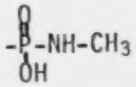
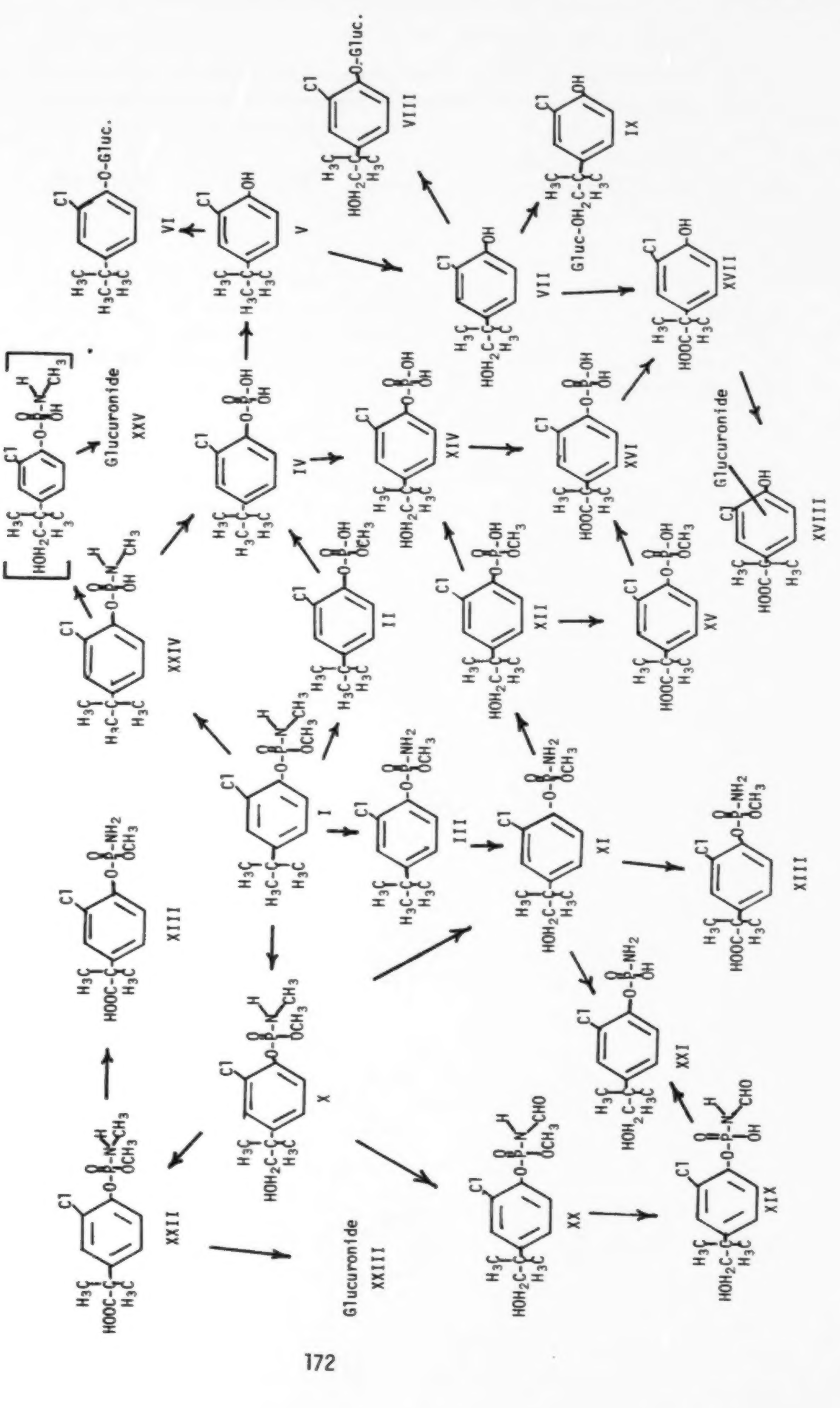
I	 $\mathrm{CH_3-\overset{CH_3}{\underset{CH_3}{C}}-}$		 $\mathrm{-\overset{O}{\underset{OCH_3}{P}}-NH-CH_3}$
II	 $\mathrm{CH_3-\overset{CH_3}{\underset{CH_3}{C}}-}$		 $\mathrm{-\overset{O}{\underset{OCH_3}{P}}-OH}$
III	 $\mathrm{CH_3-\overset{CH_3}{\underset{CH_3}{C}}-}$		 $\mathrm{-\overset{O}{\underset{OCH_3}{P}}-NH_2}$
IV	 $\mathrm{CH_3-\overset{CH_3}{\underset{CH_3}{C}}-}$		 $\mathrm{-\overset{O}{\underset{OH}{P}}-OH}$
V	 $\mathrm{CH_3-\overset{CH_3}{\underset{CH_3}{C}}-}$		
VI	 $\mathrm{CH_3-\overset{CH_3}{\underset{CH_3}{C}}-}$		
VII	 $\mathrm{HO-CH_2-\overset{CH_3}{\underset{CH_3}{C}}-}$		
VIII	 $\mathrm{HO-CH_2-\overset{CH_3}{\underset{CH_3}{C}}-}$		

	A	B	C
IX	 $\mathrm{Gluc{-}O{-}CH_2{-}\overset{CH_3}{\underset{CH_3}{C}}{-}}$		
X	 $\mathrm{HO{-}CH_2{-}\overset{CH_3}{\underset{CH_3}{C}}{-}}$		 $\mathrm{-\overset{O}{\underset{OCH_3}{P}}{-}NH{-}CH_3}$
XI	 $\mathrm{HO{-}CH_2{-}\overset{CH_3}{\underset{CH_3}{C}}{-}}$		 $\mathrm{-\overset{O}{\underset{OCH_3}{P}}{-}NH_2}$
XII	 $\mathrm{HO{-}CH_2{-}\overset{CH_3}{\underset{CH_3}{C}}{-}}$		 $\mathrm{-\overset{O}{\underset{OCH_3}{P}}{-}OH}$
XIII	 $\mathrm{HOOC{-}\overset{CH_3}{\underset{CH_3}{C}}{-}}$		 $\mathrm{-\overset{O}{\underset{OCH_3}{P}}{-}NH_2}$
XIV	 $\mathrm{HO{-}\overset{CH_3}{\underset{CH_3}{C}}{-}}$		 $\mathrm{-\overset{O}{\underset{OH}{P}}{-}OH}$
XV	 $\mathrm{HOOC{-}\overset{CH_3}{\underset{CH_3}{C}}{-}}$		 $\mathrm{-\overset{O}{\underset{OCH_3}{P}}{-}OH}$
XVI	 $\mathrm{HOOC{-}\overset{CH_3}{\underset{CH_3}{C}}{-}}$		 $\mathrm{-\overset{O}{\underset{OH}{P}}{-}OH}$

	A	B	C
XVII	$\mathrm{HOOC{-}\overset{CH_3}{\underset{CH_3}{C}}{-}}$		
XVIII	$\mathrm{HOOC{-}\overset{CH_3}{\underset{CH_3}{C}}{-}}$		(phenyl or carboxyl gluc.)
XIX	$\mathrm{HO{-}CH_2{-}\overset{CH_3}{\underset{CH_3}{C}}{-}}$		$\mathrm{-\overset{O}{\underset{OH}{P}}{-}NH{-}CHO}$
XX	$\mathrm{HO{-}CH_2{-}\overset{CH_3}{\underset{CH_3}{C}}{-}}$		$\mathrm{-\overset{O}{\underset{OCH_3}{P}}{-}NH{-}CHO}$
XXI	$\mathrm{HO{-}CH_2{-}\overset{CH_3}{\underset{CH_3}{C}}{-}}$		$\mathrm{-\overset{O}{\underset{OH}{P}}{-}NH_2}$
XXII	$\mathrm{HOOC{-}\overset{CH_3}{\underset{CH_3}{C}}{-}}$		$\mathrm{-\overset{O}{\underset{OCH_3}{P}}{-}NH{-}CH_3}$
XXIII	$\mathrm{Gluc{-}O{-}\overset{O}{C}{-}\overset{CH_3}{\underset{CH_3}{C}}{-}}$		$\mathrm{-\overset{O}{\underset{OCH_3}{P}}{-}NH{-}CH_3}$
XXIV	$\mathrm{CH_3{-}\overset{CH_3}{\underset{CH_3}{C}}{-}}$		$\mathrm{-\overset{O}{\underset{OH}{P}}{-}NH{-}CH_3}$

	A	B	C
XXV	 $\text{Gluc-O-CH}_2\text{-C(CH}_3\text{)}_2\text{—}$		 $\text{-P(=O)(OH)-NH-CH}_3$

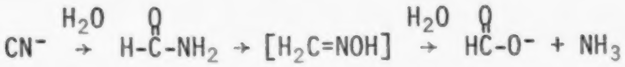

I
II
III
IV
V
VI
VII
VIII
IX
X
XI
XII
XIII
XIV
XV
XVI
XVII
XVIII
XIX
XX
XXI
XXII
Glucuronide XXIII
XXIV
Glucuronide XXV
Glucuronide
O-Gluc.
Gluc-OH₂C

CYANIDE

When rats were administered KCN by subcutaneous injection, thiocyanate was excreted in the urine. There were no significant differences between male and female rats nor was there a significant difference in thiocyanate excretion after 8 weeks of study (Mehta and McGinity, 1977).

Rhizosphere samples from field-grown tapioca plants were plated in an effort to isolate microorganisms tolerant to cyanide. Two unidentified Gram-negative rod-shaped bacteria, a *Streptomyces* sp., and two fungi identified as *Aspergillus* sp. and *Rhizopus nigricans* were isolated (Sadasivam, 1974).

An active system capable of metabolizing cyanide was obtained from mesocarp of loquat. At least three enzymes are involved. When ^{14}C-NaCN was incubated with the enzymes, paper chromatography with three solvent systems indicated the presence of formamide and formate. A third compound is believed to be formaldoxime (Shirai, 1977; Shirai et al., 1977).



$$CN^- \xrightarrow{H_2O} H\text{-}\overset{\overset{O}{\|}}{C}\text{-}NH_2 \rightarrow [H_2C{=}NOH] \xrightarrow{H_2O} H\overset{\overset{O}{\|}}{C}\text{-}O^- + NH_3$$

The reaction of CN^- with glucose was found to be pseudo-first order and pH dependent. The reaction products were biodegradable. Heterogeneous bacteria metabolized $^{14}C\text{-}CN^-$ as indicated by $^{14}CO_2$ released (Raef et al., 1977a and b).

CYANOFENPHOS (Surecide) [O-p-Cyanophenyl O-ethyl phenylphosphonothioate]

Rats, orally administered ^{14}C-cyanofenphos, excreted over 90% of the dose within one day and almost all of it within 3 days. About 97% of the excreted material was in the urine with very little difference between (+)-, (-)- and (±)- cyanofenphos administration. The major metabolites in urine were 4-cyanophenol and its sulfate. Desethylcyanofenphos was also observed in small amounts. No oxon or unreacted cyanofenphos was detected in urine. When cyanofenphos was incubated with a rat liver microsome-NADPH system, cyanofenphos oxon was formed in addition to p-cyanophenol and desethylcyanofenphos. Hydrolysis studies indicated the presence of two enzyme systems, one of which is a MFO unaffected by addition of $CaCl_2$ and TEPP. This enzyme catalyzed oxidation to the oxon and cleavage of the P-O bonds. The other enzyme was inhibited by EDTA, enhanced by $CaCl_2$, but unaffected by TEPP. This system was remarkable in hydrolyzing the (-)-oxon isomer versus the (+)-isomer (Ohkawa et al., 1977b).

When fed to cows, cyanofenphos was converted to the oxon. Residue levels in milk and tissues were very low. Levels were highest in fat and decreased in order fat >> liver > kidney ≥ muscle (Miyamoto et al., 1977a).

Rice stem borer larvae metabolized both optical isomers of cyanofenphos to the oxon, desethyl analog, 4-cyanophenol, and 4-cyanophenylglucoside. The latter was inferred from hydrolysis by β-glucosidase. The rate of metabolism of the optical isomers of cyanofenphos and its metabolites varied. Desethylcyanofenphos oxon also was observed after cyanofenphos oxon injection into rice stem borer larvae (Ohkawa et al., 1978a).

Bifoliate bean seedlings of Phaseolus vulgaris L. were treated with cyanofenphos-^{14}CN. In water culture, very little cyanofenphos was taken up through the roots and almost all radioactivity was recovered as the parent compound. When applied to the leaf surface, slow degradation occurred. After 7 days, about 22% of the radioactivity was accounted for by the desethyl analog and 4-cyanophenol. No oxon was observed. When the oxon was applied, degradation occurred rapidly to p-cyanophenol and the desethyl-oxon. These studies indicated that degradation of cyanofenphos to the oxon does not occur in the plant or that, if it does occur, oxon degradation is extremely rapid. The half-life of cyanofenphos was estimated to be about two weeks. On TLC plates, exposure of cyanofenphos to UV produced the oxon, 4-cyanophenol, and desethyl cyanofenphos. The desethyl-oxon may also be present (Chiba et al., 1976).

In acetone and in the presence of air, UV-irradiation of cyanofenphos produced the oxon, 4-cyanophenol, 4-cyanobenzoic acid, 2-hydroxy-5-cyanobenzoic acid, a hydroxylated product of the oxon, CO_2, HCN, and O-ethyl phenylphosphoric acid. In water solution only the oxon and 4-cyanophenol were identified. The main product, not identified, appeared to be the hydroxylated product of 4-cyanophenol. On silica gel TLC plates, decomposition was rapid. Identified compounds included the oxon, 4-cyanophenol, and 2-hydroxybenzoic acid. On soil thin-layer plates, cyanofenphos half-life was about 2 days when exposed to sunlight. The oxon and 4-cyanophenol were the major products (Mikami et al., 1976).

CYANOX [*O*,*O*-Dimethyl *O*-4-cyanophenyl phosphorothioate]

^{14}C-Cyanox was administered to male Wistar rats. Very little $^{14}CO_2$ was expired. Neither cyanox nor cyanoxon was detected in the 4-day pooled urine. TLC indicated five metabolites, four of which cochromatographed in various solvents with (1) demethylcyanox, (2) demethylcyanoxon, (3) *p*-cyanophenol, and (4) *p*-cyanophenyl sulfate. In the liver, cyanox, demethylcyanox, cyanoxon, demethylcyanoxon and *p*-cyanophenyl sulfate were found (Miyamoto et al., 1972).

Bifoliate bean seedlings (*Phaseolus vulgaris* L.) were exposed to cyanox by immersion of roots in a flask containing cyanox-^{14}CN. After 9 days, about 48% of the original radioactivity remained in the form of cyanox and its desmethyl analog in about equal amounts. The desmethyl compound and 4-cyanophenol were found in all parts of the plant, indicating uptake and translocation. Cyanoxon and its desmethyl analog were not confirmed. When the leaves were treated, in addition to unchanged cyanox, the organo-soluble fraction contained the cyanoxon, desmethylcyanox, desmethylcyanoxon, and 4-cyanophenol. The half-life of cyanox was one day or less, depending on the temperature. When injected into the stem, cyanox gave rise to cyanoxon, desmethylcyanox, 4-cyanophenol and perhaps desmethylcyanoxon; desmethylcyanox gave 4-cyanophenol but not the oxon; and cyanoxon gave desmethylcyanoxon and 4-cyanophenol. Exposure of cyanox on TLC-plates to sunlight or UV produced a small amount of cyanoxon only (Chiba et al., 1976).

Photodecomposition products from cyanox are summarized in the following table.

	UV	Sunlight		
Product	Acetone Solution	Water Solution	Silica Gel Plates	Soil TL-plates
Cyanoxon	+	+	+	+
Desmethylcyanox				
Desmethylcyanoxon	+	+	+	+
4-cyanophenol	+	+	+	+
4-cyanobenzoic acid	+			
2-hydroxy-5-cyanobenzoic acid	+			
CO_2	+			
HCN	+			

(Mikami et al., 1976)

CYCLOPHOSPHAMIDE (NSC-26271, CP, Cytoxan, Endoxan, N,N-Bis(β-chloroethyl)-N',O-propylene phosphoric acid) [2-Bis(2-chloroethylamino)-tetrahydro-2H-1,3,2-oxazaphosphorine-2-oxide]

In mice exposed to CP, the hydroxylated intermediate (4-hydroxy CP) was metabolized to carboxyphosphamide. The 4-ketophosphamide was also found. These two compounds were the major metabolites in man, rats, rabbits, dogs and sheep (Alarcon and Meinenhofer, 1971; Bakke et al., 1972; Hill et al., 1970; Norpoth et al., 1972; Struck et al., 1971; Takamizawa et al., 1972). Other metabolites in smaller amounts also observed included: hydracrylic acid, 3-hydroxy-propionamide, 3-phosphorylpropionic acid and the oxazaphosphorine-2-oxide (XVIII) (Bakke et al., 1972; Struck et al., 1971).

The microsomal metabolism of cyclophosphamide was also studied with liver preparations. Breakdown apparently proceeded first via 4-HO analog. The tautomer, aldophosphamide, then yielded phosphoramide mustard by elimination of acrolein. 4-Hydroxycyclophosphamide and aldophosphamide were also converted to the 4-keto analog and carboxyphosphamide, respectively. Two other metabolites were identified as 2-(2-chloroethylamino)tetrahydro-2H-1,3,2-oxazaphosphorine-2-oxide and 3-hydroxypropyl-N,N-bis(2-chloroethyl) phosphorodiamidate (Connors et al., 1974).

Acid hydrolysis of cyclophosphamide yielded N-(2-chloroethyl)-N'-(3-phosphatopropyl)ethylenediamine, N-(2-hydroxyethyl)-N'-(3-phosphatopropyl)ethylenediamine, and the principal ultimate product N'-(3-hydroxypropyl)ethylenediamine (Friedman et al., 1965; Chakrabarti and Friedman, 1973).

The metabolism of cyclophosphamide has been summarized in the following table. Where known, the organism degrading cyclophosphamide, the mode of administration, and analytical procedures used are given.

Metabolite	Organism	Admin.	Source	Anal.	Reference
II	Rat (Sprague-Dawley)	i.v.	urine	electro-phoresis, MS,PC	Schaumloffel & Wetzel, 1978
	Rat[4] (♂ Wistar)	i.p.	urine	MS	Cox et al., 1978
			H.m.[1]	MS	Cox et al., 1978
	Mouse[5] (♀ BALB/c)	i.p.	urine	MS	Cox et al., 1978
			H.m.	MS	Cox et al., 1978
	Rabbit[4] (Dutch)	i.p.	urine	MS	Cox et al., 1978
			H.m.	MS	Cox et al., 1978
III	Sheep	oral	urine		Bakke et al., 1971
	Sheep	oral	urine	MS,IR	Bakke et al., 1972
	Rabbit	i.p.	urine	MS,NMR	Takamizawa et al., 1972
	Dog (beagle)	i.v.	urine	MS,IR	Hill et al., 1970
	Dog (beagle)	i.v.	urine	MS,NMR	Struck et al., 1971
	Rat		H.m.	MS,IR	Connors et al., 1974
	Rat (♂)		H.m.	TLC	Sladek, 1973
	Mouse		H.m.	TLC	Sladek, 1973
	Rat (♂)		L.s.[2]	PC[3]	Hohorst et al., 1971
	Rat[4] (♂ Wistar)	i.p.	urine	MS	Cox et al., 1978
			H.m.	MS	Cox et al., 1978
	Mouse[5] (♀ BALB/c)	i.p.	urine	MS	Cox et al., 1978
			H.m.	MS	Cox et al., 1978
	Rabbit[4] (Dutch)	i.p.	urine	MS	Cox et al., 1978
			H.m.	MS	Cox et al., 1978
	Rat (Sprague-Dawley)	i.v.	urine	electro-phoresis, PC,MS	Schaumloffel & Wetzel, 1978
	Rat		urine		Norpoth et al., 1972
	Human	i.v.	urine	electro-phoresis, PC,MS	Schaumloffel & Wetzel, 1978

Metabolite	Organism	Admin.	Source	Anal.	Reference
V	Rat		H.m.	IR,MS	Connors et al., 1974
	Rat (♂)		H.m.	TLC	Sladek, 1973
	Mouse		H.m.	TLC	Sladek, 1973
	Sheep	oral	urine	MS,IR	Bakke et al., 1972
Va	Human	i.v.	urine	Radiochromatog	DeVita & Adamson, 1970
	Human	i.p.	urine	Chromatog	Hohorst et al., 1965
	Rat	i.p.	serum	Chromatog	Hohorst et al., 1965
VI	Mouse		H.m.	MS	Hill et al., 1972
	Rat (Sprague-Dawley)	i.v.	urine	electrophoresis, MS, PC	Schaumloffel & Wetzel, 1978
VII	Sheep	oral	urine		Bakke et al., 1971
		oral	urine	MS,IR	Bakke et al., 1972
	Rabbit	i.p.	urine	MS,IR	Takamizawa et al., 1972
	Dog (beagle)	i.v.	urine	MS,NMR	Struck et al., 1971
	Dog		urine	TLC,MS,IR	Struck, 1971
	Mouse		H.m.	MS	Hill et al., 1972
			H.m.	IR,MS	Connors et al., 1974
	Rat (Sprague-Dawley)	i.v.	urine	electrophoresis, MS,PC	Schaumloffel & Wetzel, 1978
			urine		Norpoth et al., 1972
	Human	i.v.	urine	electrophoresis, MS,PC	Schaumloffel & Wetzel, 1978
	Rat[4] (♂ Wistar)	i.p.	urine	MS	Cox et al., 1978
			H.m.	MS	Cox et al., 1978
	Mouse[5] (♀ BALB/c)	i.p.	urine	MS	Cox et al., 1978
			H.m.	MS	Cox et al., 1978
	Rabbit[4] (Dutch)	i.p.	urine	MS	Cox et al., 1978
			H.m.	MS	Cox et al., 1978

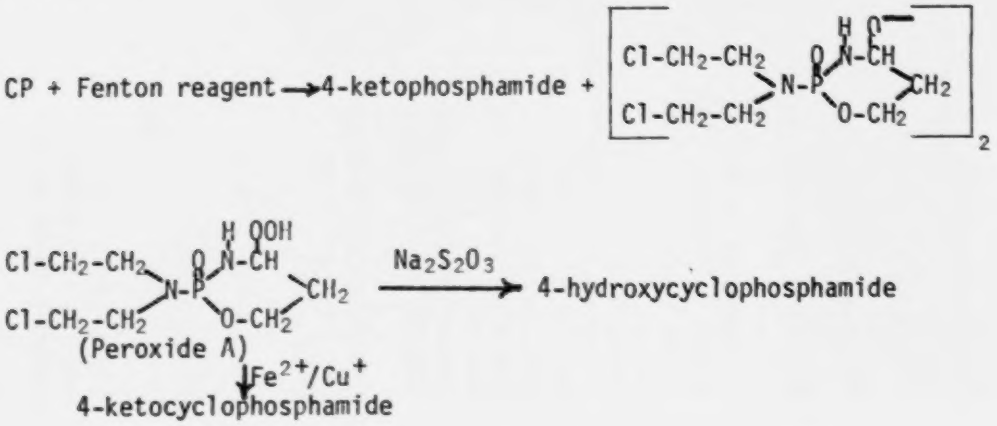
Metabolite	Organism	Admin.	Source	Anal.	Reference
VIIa	Rat		H.m.		Rauen et al., 1968
VIIb	Sheep	oral	urine	MS,IR	Bakke et al., 1972
VIII	Ascites tumor cells			Chemical	Grunicke et al., 1965
	Rat (♂)		H.m.	TLC	Sladek, 1973
	Mouse		H.m.	TLC	Sladek, 1973
	Dog (beagle)	i.v.	urine	MS,IR	Hill et al., 1970
XII	Rabbit (Angora)	oral	urine	TLC	Renerre et al., 1975
	Human	i.v.	urine	TLC,MS	Cox & Levin, 1975
		i.v.	urine	Radio-chromatog	DeVita & Adamson, 1970
	Rat	i.p.	serum	Chromatog	Hohorst et al., 1965
		i.p.	serum	Chromatog	Brock & Hohorst, 1967
XIII	Rat	i.p.	serum	Chromatog	Brock & Hohorst, 1967
			H.m.		Rauen et al., 1968
XIV	Human			TLC,MS	Cox & Levin, 1975
XV	Rat		H.m.		Rauen et al., 1968
			serum		Rauen & Norpoth, 1967
XVI	Rat (Sprague-Dawley)	i.v.	urine	Electro-phoresis, MS,PC	Schaumloffel & Wetzel, 1978
	Mouse		H.m.	MS	Colvin et al., 1973
	Rat^4 (♂ Wistar)	i.p.	urine	MS	Cox et al., 1978
			H.m.	MS	Cox et al., 1978
	Mouse^5 (♀ BALB/c)	i.p.	urine	MS	Cox et al., 1978
			H.m.	MS	Cox et al., 1978
	Rabbit^4 (Dutch)	i.p.	urine	MS	Cox et al., 1978
			H.m.	MS	Cox et al., 1978

Metabolite	Organism	Admin.	Source	Anal.	Reference
XVIII	Sheep	oral	urine	MS,IR	Bakke et al., 1972
XIX	Rat		H.m.		Alarcon & Meienhofer, 1971
XXII	Human	i.v.	urine	Radio-chromatog	DeVita & Adamson, 1970
XXIII	Rat	i.p.	serum	Electrophoresis	Rauen & Norpoth, 1967
XXV	Rat		H.m.	MS,IR	Connors et al., 1974
	Sheep	oral	urine	MS,IR	Bakke et al., 1972
	Rat[4] (♂ Wistar)	i.p.	urine	MS	Cox et al., 1978
			H.m.	MS	Cox et al., 1978
	Mouse[5] (♀ BALB/c)	i.p.	urine	MS	Cox et al., 1978
			H.m.	MS	Cox et al., 1978
	Rabbit[4] (Dutch)	i.p.	urine	MS	Cox et al., 1978
			H.m.	MS	Cox et al., 1978
XXVI	Human	i.v.	urine	TLC,MS	Cox & Levin, 1975
XXIX	Dog		urine	Chromatog, Electrophoresis	Hill, 1971
XXX	Mouse		H.m.	Chromatog, Electrophoresis	Hill, 1971

[1] H.m. = Hepatic microsomes
[2] L.s. = Liver slices
[3] PC = Paper chromatography

[4] Metabolism by microsomes favored S-enantiomers
[5] Metabolism by microsomes favored R-enamtiomers

The reaction of cyclophosphamide in nonbiological systems is summarized.


CP + Fenton reagent → 4-ketophosphamide +
Cl-CH2-CH2
Cl-CH2-CH2
N-P
O
H
N-CH
CH2
O-CH2
2
Cl-CH2-CH2
Cl-CH2-CH2
N-P
O
H OOH
N-CH
CH2
O-CH2
Na2S2O3
4-hydroxycyclophosphamide
(Peroxide A)
Fe2+/Cu+
4-ketocyclophosphamide

(Takamizawa et al., 1974)

$$\begin{tikzcd} \text{CP} \arrow[r, "\text{Aq. }KMnO_4"] \arrow[d, "KMnO_4"', "\text{rat urine}"] & \underset{\text{III}}{\text{4-ketophosphamide}} + \text{Compound XXV} \\ \text{III \& VII} & \end{tikzcd}$$

(Jarman, 1973)

(Norpoth et al., 1972)

$$\text{Peroxide A} \xrightarrow{\text{Fenton Reagent}} \text{4-hydroxyphosphamide}$$

(van der Steen et al., 1973)

$$\left.\begin{array}{l} \text{CP} + H_2O_2 \\ \text{CP} + FeSO_4 \\ \text{CP} + FeSO_4 + \text{EDTA} \\ \text{CP} + FeSO_4 + \text{EDTA} + H_2O_2 \\ \text{CP} + FeSO_4 + \text{ascorbic acid} \\ \text{CP} + FeSO_4 + H_2O_2 + \text{ascorbic acid} \\ \text{CP} + CuSO_4 + \text{sodium ascorbate} \end{array}\right] \rightarrow \text{acrolein}$$

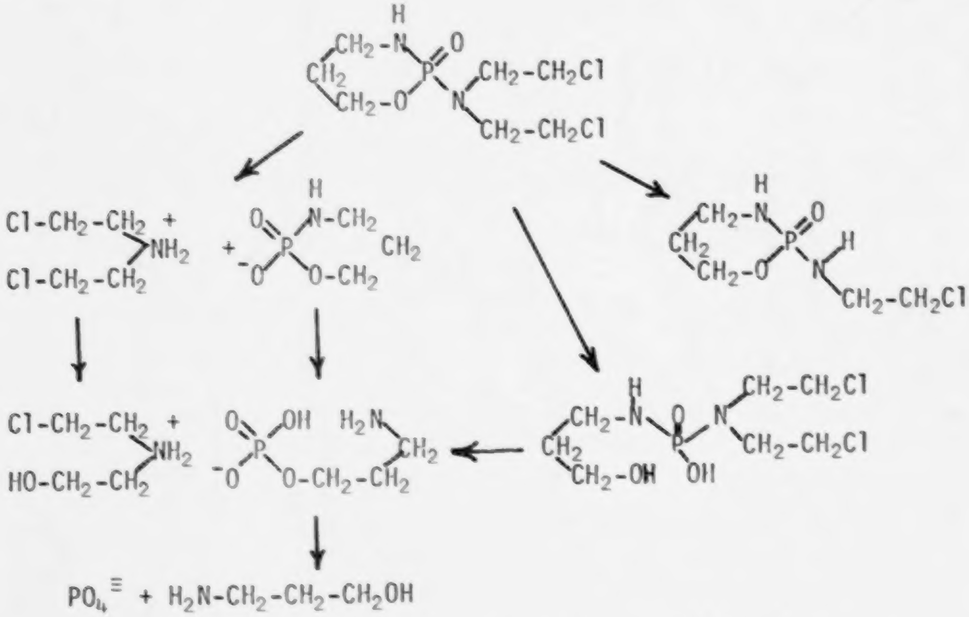
(Alarcon and Meienhofer, 1971)

Hydrolysis

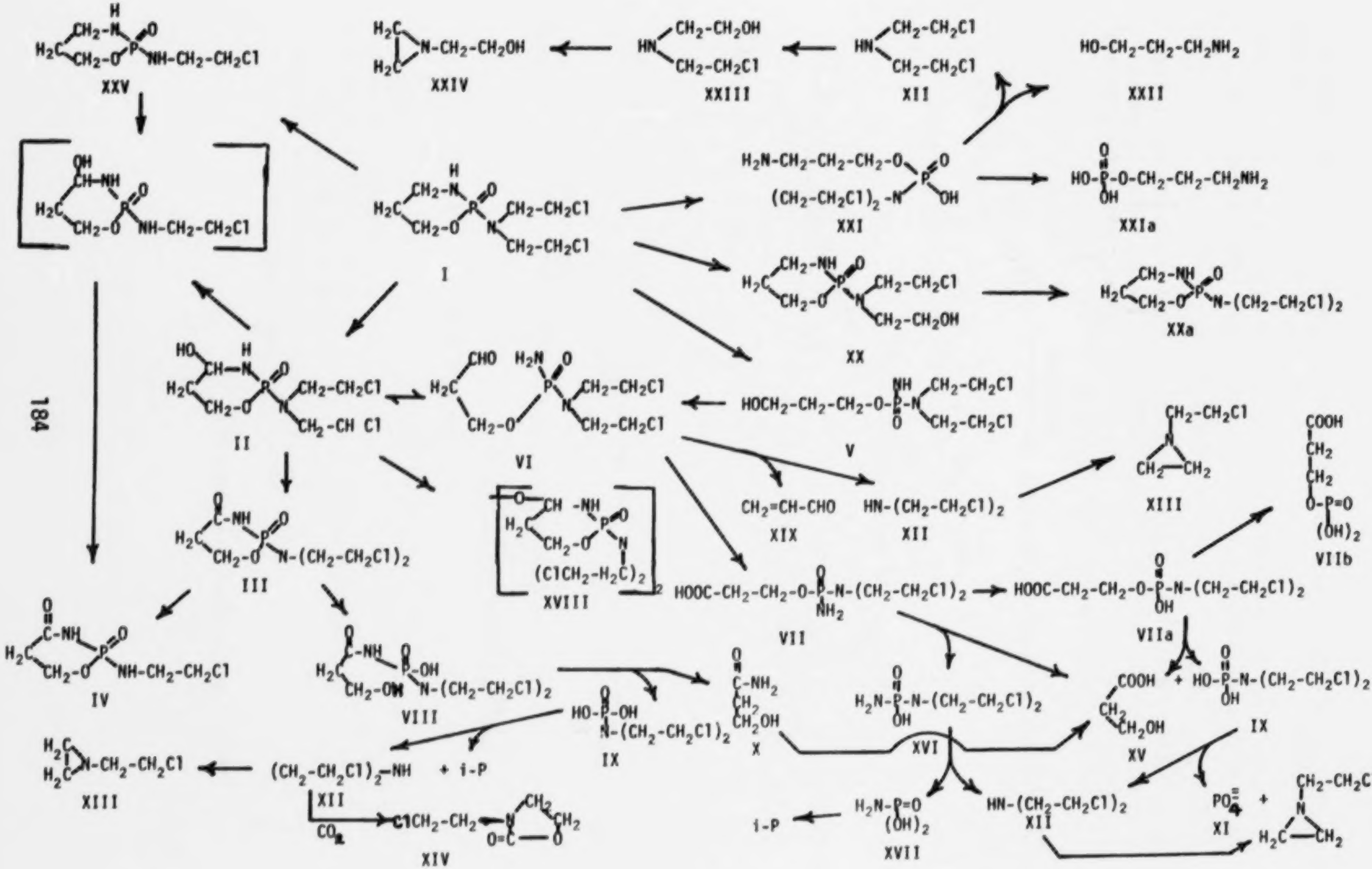
In neutral pH, the main product is compound VII (Hirata et al., 1967). At pH 8.6, compounds XII and XXIa were formed (Arnold and Klose, 1960).

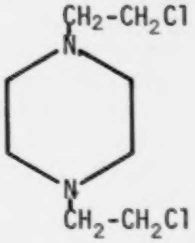
When heated to reflux in distilled water, cyclophosphamide yielded compounds XXVII, XXVIII, XXX, and XXXI (Friedman, 1967; Friedman et al., 1965). Other studies also showed the presence of compounds XXX and XXXI (Chakrabarti and Friedman, 1973).

At pH = 2

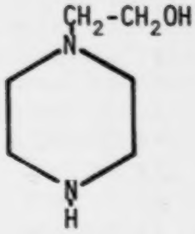


(Arnold and Klose, 1961)

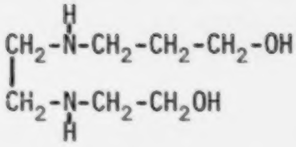

XXV
XXIV
XXIII
XII
XXII
I
XXI
XXIa
XX
XXa
II
VI
V
III
XVIII
XIX
XII
XIII
VIIb
IV
VIII
VII
VIIa
IX
X
XVI
XV
XIII
XII
i-P
CO2
XIV
XVII
XI



XXVI

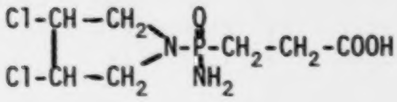


XXVII

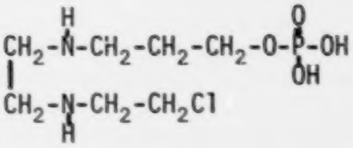


$$\begin{array}{l}\mathrm{CH_2\text{-}\overset{H}{N}\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}OH}\\ |\\ \mathrm{CH_2\text{-}\underset{H}{N}\text{-}CH_2\text{-}CH_2OH}\end{array}$$

XXVIII

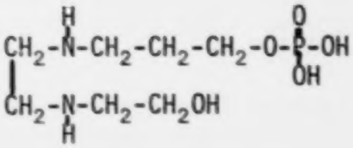


XXIX



$$\begin{array}{l}\mathrm{CH_2\text{-}\overset{H}{N}\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}O\text{-}\overset{O}{\underset{OH}{P}}\text{-}OH}\\ |\\ \mathrm{CH_2\text{-}\underset{H}{N}\text{-}CH_2\text{-}CH_2Cl}\end{array}$$

XXX



$$\begin{array}{l}\mathrm{CH_2\text{-}\overset{H}{N}\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}O\text{-}\overset{O}{\underset{OH}{P}}\text{-}OH}\\ |\\ \mathrm{CH_2\text{-}\underset{H}{N}\text{-}CH_2\text{-}CH_2OH}\end{array}$$

XXXI

CYCLOPRATE (Zardex, ZR-856) [Hexadecyl cyclopropanecarboxylate]

The fate of ^{14}C-carboxyl-cycloprate was studied in rat, cow and dog. The main metabolite excreted by rats was obtained from urine and identified as N-(cyclopropylcarbonyl)glycine (CPCA-glycine) (9%). O-(cyclopropylcarbonyl)carnitine (CPCA-carnitine) was present in the urine at 2%. After hydrolysis of the ester, a series of ω-cyclopropyl fatty acids were formed and handled like natural fatty acids, i.e., converted to glycerides. 13-Cyclopropyltridecanoic and 15-cyclopropylpentadecanoic acids were identified from liver. 11-cyclopropylundecanoic acid was also indicated on TLC but not isolated for spectral identification (Quistad et al., 1977 and 1978a; Schooley et al., 1978).

A lactating cow, given a single oral dose of cycloprate, excreted 89% of the applied dose in urine, 5% in feces, and 6% in milk. About 65% of the dose was excreted in urine within 7 days as CPCA-glycine and 7% as free CPCA. CPCA-carnitine was present as the primary metabolite in milk and muscle (0.04-0.06 ppm). Milk also contained triacylglycerols and a series of saturated ω-cyclopropyl fatty acids (C_8 - C_{18}). The 13-cyclopropyltridecanoic acid accounted for about half of these acids (Quistad et al., 1978c).

Beagle dogs were given a single oral dose of ^{14}C-carboxyl-cycloprate. About 25% was excreted via urine and 2% in feces. The remainder was retained in muscle (56%), kidney (7%), adipose tissue (6%), hide (6%), and liver (2%). The major metabolite in muscle was CPCA-carnitine. More than 60% of the residue in adipose tissue and hide was in the form of ω-cyclopropyl fatty acids as triacylglycerols. The major component was 13-cyclopropyltridecanoic acid. In liver and kidney, these ω-acids were as phospholipids. CPCA-glycine (24%) and CPCA-carnitine (58%) were observed in urine. From kidneys 13-cyclopropyltridecanoic acid and 15-cyclopropylpentadecanoic acid were observed as free acids and in the phosphoglycerides. In tissues of dogs, 11-cyclopropylundecanoic acid, 13-cyclopropyltridecanoic acid, and 15-cyclopropylpentadecanoic acid were present in free state. In addition to these three, the 17-cyclopropylheptadecanoic acid and a longer acid were present as triacylglycerols. CPCA was also present as a triacylglycerol (Quistad et al , 1978d).

When applied to plants, cycloprate formed polar conjugates of cyclopropanecarboxylic acid and ω-cyclopropyl fatty acids with long chain saturated and unsaturated carbon chains (Quistad et al., 1977). Analysis of foliage and fruit cuticle of apple and orange trees showed the presence of monoenoic and some trienoic acids but not dienoic acids. 15-Cyclopropylpentadecanoic acid, several isomers of 15-cyclopropylpentadecenoic acids and small amounts of 17-cyclopropylheptadecenoic acid were observed (Quistad et al., 1978b; Schooley et al., 1978).

The fungus Fusarium oxysporum degraded cyclopropanecarboxylic acid through an intermediate, identified as the carnitine derivative, to γ-hydroxybutyric acid (Guilbert and Chung, 1974; Schiller and Chung, 1970).

CYOLANE (Phosfolan; Ethylene (diethoxyphosphinyl)-dithioimidocarbonic acid) [2-(Diethoxyphosphinylimino)-1,3-dithiolan]

About 50% of an orally administered dose of ^{14}C-cyolane was excreted and 20% respired by rats within 6 days. The only metabolite occurring in significant amounts in urine and tissue was identified as thiocyanate (Kapoor and Blinn, 1977).

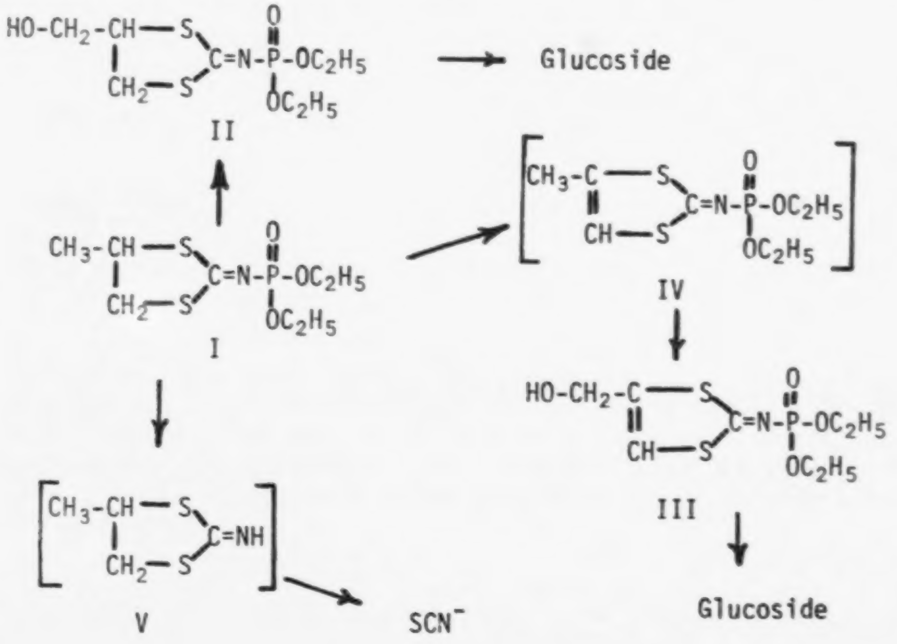
When applied to cotton leaves or glass surfaces, phosfolan degraded rapidly. In the presence of light and air, most of this pesticide degraded within a week. Disappearance from cotton leaves was enhanced by movement into the leaf (Belal et al., 1978).

CYTROLANE (Mephosfolan) [Propylene(diethoxyphosphinyl)dithioimidocarbonate]

In the urine of rats dosed with cytrolane, TLC and MS indicated that the methyl moiety was attacked to produce carboxylic ions. Hydrolysis of the P-N bond was followed by ring opening and release of thiocyanate. The latter was the main tissue metabolite (Kapoor, 1978).

^{14}C-Cytrolane (I), labeled at the imino carbon, was applied to leaves of cotton plants. After 42 days, about 60% of the label was recovered as unchanged cytrolane. A minor metabolite, compound II, and major metabolite III were isolated as glucosides. Identification of the aglycones was made after hydrolysis of the glucosidic moiety with β-glucosidase. Another minor metabolite was identified as thiocyanate. Other observed metabolites were not identified (Zulalian and Blinn, 1977). The hydroxymethyl and its glucoside were also observed in other studies with cotton (Kapoor, 1978).

When ^{14}C-labeled cytrolane was applied to rice, about 91% of the residue was unchanged material. The remainder of the radioactivity was composed of about 17 metabolites. Unextractable radioactivity was believed to be in the form of ^{14}C-labeled cellulose, lignin and starch (Ku and Kapoor, 1977; Ku et al., 1978). Fish kept in the rice paddy metabolized cytrolane to thiocyanate and many other metabolites (Kapoor, 1978; Ku et al., 1978).



2,4-D and RELATED COMPOUNDS

2,4-D	[2,4-Dichlorophenoxyacetic acid]
2,4-DB	[4-(2,4-Dichlorophenoxy)butyric acid]
Erbon	[2-(2,4,5-Trichlorophenoxy)ethyl 2,2-dichloropropionate]
MCPA	[4-Chloro-2-methylphenoxyacetic acid]
Silvex	[2-(2,4,5-Trichlorophenoxy)propionic acid]
2,4,5-T	[2,4,5-Trichlorophenoxyacetic acid]
CPA	[Chlorophenoxyacetic acid]

2,4-D [2,4-Dichlorophenoxyacetic acid]

The concentration of 2,4-D in plasma and urine was determined after oral ingestion of 5 mg/kg 2,4-D by human male volunteers. Elimination from plasma exhibited first-order rate and a $t_{1/2}$ of 11.6 h; $t_{1/2}$ of urinal elimination was 17.7 h. Urinary excretion of 2,4-D was primarily in unchanged form (82.3%) but a small amount (12.8%) was in the form of an unidentified conjugate (Sauerhoff et al., 1977a).

Rats orally dosed with 2,4-D converted the 2,4-D to the glycine and taurine conjugates (Grunow and Bohme, 1974).

Proton magnetic resonance studies indicated that 2,4-D binds to bovine serum albumin and that the methylene protons are closer to the binding site than the ring protons (Haque et al., 1975). When 2,4-D amine was administered to pigs, a weak binding to plasma protein was observed. Hydrolysis studies with urine also indicated some conjugation of 2,4-D (Erne, 1966b).

The plasma half-life of 2,4-D derivatives is summarized in the following table.

2,4-D compound	Species	$T_{1/2}$ (h)
amine salt	Rat, male	2.9 ± 0.4
	Rat, female	3.3 ± 0.5
	Pig	12.0 ± 2.0
	Calf	7.5 ± 0.8
	Chicken	7.7 ± 0.7
K-Na salt	Rat, male	3.5 ± 0.5
	Calf	8.0 ± 0.6
Butyl ester	Rat, male	6.0 ± 1.0
	Pig	10.0 ± 0.8
	Calf	10.0 ± 1.0

(Erne, 1966a)

^{14}C-Labeled 2,4-D was injected into a dogfish shark (*Squalus acanthiac*) and urine was collected. Analysis by TLC and IR showed that 90-95% of the ^{14}C in the urine was in the form of a 2,4-D taurine conjugate. The remainder was unchanged 2,4-D (James and Bend, 1976; Guarino, et al., 1977). About 70% of the dose was eliminated in urine within 4-6 days after treatment.

	$t_{1/2}$
Plasma	45 min
Muscle	2-3 days
Liver	ca 5 days

(Guarino et al., 1977)

Bluegills (Lepomis machrochirus) were exposed for 12 weeks to ring labeled ^{14}C-2,4-D dimethylamine salt in an outdoor pool. Analyses indicated that ^{14}C fragments were incorporated into natural products: fatty acids, free and in triglycerides; glycogen; and protein. $^{14}CO_2$ was observed in a pool without fish. Other preliminary in vitro and in vivo studies showed uptake of ^{14}C-2,4-D by bluegills but no ^{14}C-metabolites were observed. These studies indicated degradation of 2,4-D by microorganisms in the pool (Stalling and Huckins, 1978).

Bluegill and channel catfish took up less than 0.5% of 2,4-D dimethylamine salt when exposed in aquaria at 2 ppm. During 7-day exposure, there was no evidence of metabolism. When this herbicide was administered i.p. to bluegills, 90% was excreted within 6 h (Sikka et al., 1977). Detoxication studies were conducted with mosquito fish (Gambusia affinis) and ethyl and n-butyl ester of 2,4-dichlorophenoxythioloacetic acid. Both esters were hydrolyzed by esterases in livers and gills (Chambers et al., 1977).

Phytophthora megasperma var. sojae and cell suspensions of white clover (Trifolium repens) were not able to metabolize 2,4-D but did degrade 2,4-DB by a path not including β-oxidation (Smith and Phillips, 1976; Smith and Oswald, 1978).

Nearly all of 2,4-D applied to cereal plants remained in treated leaves and did not move into new growth. Analyses indicated that 2,4-D was bound mainly to proteins with a relative electrophoretic mobility of 0.023 (70%) and to proteins with electrophoretic mobilities of 0.50 (15%) and 0.54 (15%). Hydroxylated metabolites of 2,4-D were also present, both free and conjugated with nonprotein material (not further characterized) which was probably glucose (Zemskaya et al., 1977).

Wheat callus tissue was cultured in medium with 2,4-D. Analyses indicated the presence of the following metabolites with 4-HO-2,5-D as the main metabolite. 4-HO-2,5-D, 4-HO-2,3-D, and 4-HO-2-CPA were present as sugar conjugates. After 6-8 days, ring hydroxylation and subsequent conjugation with sugars was the major pathway for 2,4-D metabolism. Over 37% of the added label was present as water-soluble and ether-insoluble compounds in the plant tissue cells. Radiolabel in the form of ether-soluble amino acid conjugates and bound to insoluble cellular tissue was also present (Bristol et al., 1977).

In rice root callus tissue, after 7 days the major metabolites in the water-soluble fraction seemed to be sugar esters of 2,4-D. Two aglycones found were 4-HO-2,3-D and 4-HO-2,5-D. Amino acid conjugates were not detected (Feung et al., 1976).

The nature of the connection of 2,4-D with corn leaf proteins was investigated. The bonds were broken only by urea solutions, indicating that hydrogen bonds were formed in the 2,4-D-protein complex (Zemskaya et al., 1976).

2,4-D was metabolized rapidly, 60% in 20 days, in milkweed leaves above the treated leaves, whereas no detectable 2,4-D metabolism was detected in hemp dogbane roots after 20 days (Wyrill and Burnside, 1976).

Wheat cells (*Triticum monococcum* L.) were incubated with 2,4-D-2^{14}C. Cells were harvested after 8 days and extracted. Analyses indicated the presence of sugar conjugates of: 2,4-D; 4-HO-2,4-D; 4-HO-2,3- and/or 5-HO-2,4-D; 4-HO-2-CPA; 6-HO-2,4-D. Amino acid conjugates were also present (Bristol et al., 1976).

2,4-D was applied to red-kidney bean (*Phaseolus vulgaris* L.), soybean [*Glycine max* (L.) Merr., var. Clay], pea (*Pisum sativum* L., var. Little Marvel), wild oat (*Avena fatua* L.), barley (*Hordeum vulgare* L., var. Larker), yellow foxtail [*Setaria glauca* (L.) Beauv.], bromegrass (*Bromus inermis* Leyss., var. Manchar Smooth), timothy (*Phleum pratense* L., var. Climax), and orchardgrass (*Dactylis glomerata* L., var. Sterling). Up to 3% of absorbed 2,4-D was converted to 2,4-dichlorophenol (2,4-DCP) within 5 days after hydroponic application. This phenol was also observed after application of 3-(2,4-dichlorophenoxy)propionic acid [3-(2,4-DP)] to orchardgrass and bromegrass (Steen, 1973; Steen et al., 1974).

Khapli wheat plants (*Triticum dicoccum* Schrank), timothy grass (*Phleum pratenese* L.), Saksa bean plants (*Phaseolus vulgaris* L.), Primorskaya 494 soybeans (*Glycine hispida* Max.), sunflower (*Helianthus annus* L.), and strawberry plants (*Fragaria grandiflora* Ehrh.) were exposed to methylene- and ring-labeled 2,4-D-^{14}C. Results are summarized in the following table (Chkanikov et al., 1976).

Soybean root callus cultures metabolized 2,4-D. Metabolites identified included 2,4-D glutamic acid (2,4-D-Glu) and 2,4-D aspartic acid conjugates; other not identified 2,4-D amino acid conjugates; 2,5-dichloro-4-hydroxyphenoxyacetic acid (4-OH-2,5-D); and 5-OH-2,4-D (Davidonis et al., 1978). In a comparison of 2,4-D metabolism by soybean callus, soybean plant and corn plants, no qualitative differences were observed. Hydroxy compounds, mainly as glucosides, were identified as 5-OH-2,4-D, 4-OH-2,3-D and 4-OH-2,5-D. Amino acid

Metabolite	PLANT					
	T. dicoccum	P. protense	Ph. vulgaris	G. hispida	H. annus	F. grandiflora
N-2,4-D L-aspartate plus L-glutamate	0	0	+	+	+	0
4-HO-2,5-D + 4-HO-2,3-D:						
Free	+	0	+	+	0	0
4-O-β-D glucoside	+	+	+	+	0	+
1-O-(2,4-D)-β-D-glucose	+	+	+	+	+	+
2,4-Dichlorophenol glycoside	+	+				+
Unidentified metabolite	+	+	+	+	0	0

(Chkanikov et al., 1976)

conjugates were identified as 2,4-D conjugates of aspartic acid, glutamic acid, alanine, valine, phenylalanine, tryptophan and leucine. There were some data that suggested the presence of amino acid conjugates of ring hydroxylated 2,4-D (Feung et al., 1978).

In beans (*Phaseolus vulgaris* L.) and soybeans (*Glycine hispida* Max.), 2,4-D was metabolized rapidly to 4-*O*-β-D-glucosides of 4-OH-2,5-D and 4-OH-2,3-D and *N*-(2,4-D) conjugates of L-aspartic acid and L-glutamic acid. Free 4-OH-2,5-D and 4-OH-2,3-D and 1-*O*-(2,4-D)-β-D-glucose were also present. Wheat plants (*Triticum dicoccum* Schrank) produced free 4-OH-2,5-D and 4-OH-2,3-D, 1-*O*-(2,4-D)-β-D-glucose, 4-*O*-β-D-glucosides of 4-OH-2,5-D and 4-OH-2,3-D, and 2,4-dichlorophenol glycoside. Timothy grass (*Phleum pratense* L.) produced the same metabolites as wheat except the free hydroxy compounds. Sunflowers (*Helianthus annus* L.) produced *N*-(2,4-D) conjugates of aspartic and glutamic acids and 1-*O*-(2,4-D)-β-D-glucose. Strawberry plants (*Fragaria grandiflora* Ehrh.) produced 1-*O*-(2,4-D)-β-D-glucose, 4-*O*-β-D-glucosides of 4-OH-2,5-D and 4-OH-2,3-D, and the glycoside of 2,4-dichlorophenol (Chkanikov et al., 1976).

Uptake of 2,4-D by the seaweeds *Ulva* sp., *Enteromorpha* sp., and *Rhodymenia* sp. was maximal after 24 h, with the total amount absorbed varying from 0.01 to 0.03% of the 2,4-D added to the culture medium. The bioaccumulation factor for these three algae was 0.001, 0.001 and 0.003, respectively. No metabolites of 2,4-D were detected when *Ulva* sp. and *Enteromorpha* sp. were exposed to ^{14}C-2,4-D for 4 days. Because of the low level of uptake, however, detection of 2,4-D metabolites would have been very difficult (Sikka et al., 1976).

Species of the fungus *Rhizoctania* produced an extracellular phenol oxidase that was capable of polymerizing 2- and 4-chlorophenol to tetrameric compounds and 2,4-dichlorophenol to a dimer (Sjoblad, 1977).

2,4-D dimethylamine salt and the octyl ester were applied to a Naff silt loam soil. After hydrolysis of the ester, the metabolic pattern of both were the same and both carboxyl-^{14}C and ring-^{14}C-2,4-D were degraded to $^{14}CO_2$ (Wilson and Cheng, 1978).

Herbicide half-life in prairie soils

Compound	$T_{1/2}$ (d)
2,4-D	< 7
2,4-DB	< 7
2,4,5-T	12
dichloroprop	10
fenoprop	12

(Smith, 1978)

In other studies with enzyme preparations from Arthrobacter sp., 2,4-D was converted to 2,4-D phenol and glyoxylate. Condensation of two glyoxylate molecules occurred with loss of CO_2 from one carboxyl group. A compound chromatographically identical to alanine was observed. With ring-labeled 2,4-D, labeled succinate was produced (Tiedje et al., 1968). Enzymes from a soil microorganism Arthrobacter sp. were used to study 2,4-D degradation. D- and L-chlorosuccinate were shown to be poor substrates and probably not intermediates between 2-chloromaleylacetate and succinate in this organism. These studies indicated that the last chlorine was removed by displacement with a hydroxyl group. In soil, 2,4-D was converted in part to 2,4-dichlorophenol. Other compounds were observed but not identified when 2,4-D was added to a fresh water and sediment system (Sharpee, 1973).

When Hendersonula toruloidea and Stachybotrys atra were grown in the presence of ^{14}C-2,4-D, about 12% of ^{14}C was in humic polymers and up to 16% in Mycelia (Wolf and Martin, 1976). The rate of hydrolysis of 2,4-D esters was determined for the methyl and butoxyethyl esters and the $t_{1/2}$ was calculated to be 1.1 and 0.6 h, respectively, at pH 9; 44 and 26 days, respectively, at pH 6. Structure-activity relationships were used to calculate $t_{1/2}$ for the propyl (17 h, 710 d), 1-butyl (5.2 h, 220 d), 1-octyl (5.2 h, 220 d), 2-octyl (37 h, 1500 d), and 2-butoxymethylethyl (4.4 h, 180 d) esters at pH 9 and 6, respectively (Zepp et al., 1975).

Degradation by soil microorganisms

pH	$T_{1/2}$ (d)	
	2,4-D	MCPA
8.5	6	5
7.5	5	5
6.3	5	6
5.5	6	5
5.0	8	13
4.5	21	>50
4.0	41	--

(Torstensson, 1974)

In photolytic studies with 2,4-D, replacement of the ortho chlorine by hydrogen accounted for more than 90% of the photoreaction in hexane and hexadecane. In water, at concentrations above 300 ppm, 2- and 4-CPA were the major photoproducts. At dilute concentration (<1 ppm), the major photoproducts were 2,4-dichlorophenol and products containing one hydroxy group in place of a chlorine (Zepp et al., 1975).

When aqueous buffered solutions of 2,4-D and riboflavin were subjected to aerobic photolysis, decomposition of 2,4-D was not detected (Silber et al., 1976).

Dichlorophenol bleed, a process waste of 2,4-D manufacture, was applied to a highly alkaline arid soil in eastern Oregon at rates up to 500 lb 2,4-D per acre. Within 600 days, concentrations of 2,4-D and dichlorophenol decreased by a factor of 10 (Goulding, 1973).

2,4-D hydrolysis, photolysis and vaporization

Ester	$T_{1/2}$			
	pH 9 (1)	pH 6 (1)	Photol. (2)	Vaporiz. (2)
Methyl	1.1 h	44 d	29 d	22.0 d
2-Propyl	17.0	710		
1-Butyl	5.2	220		1.1
1-Octyl	5.2	220		11.5
2-Octyl	37.0	1500		
2-BuOethyl	0.6	26	16	895.0
2-BuOmethylethyl	4.4	180		

(1) 28C
(2) 25C

(Zepp et al., 1974)

Fourteen weeks after treatment of eurasion watermilfoil with 2,4-D butoxyethanol ester (2,4-DBEE), there were no significant residues recovered. 2,4-DBEE degradation was greatest under high light and and temperature levels. About 50% of the 2,4-DBEE degraded in 12 h under ultraviolet light. In addition to the ethyl ester, some volatile products and other unidentified products were formed. When pond or polluted water with watermilfoil was treated with 2,4-DBEE, within 24 h all 2,4-DBEE had been converted to 2,4-D, CO$_2$, and unknown metabolites. Acid hydrolysis indicated that the unidentified metabolites were carbohydrate complexes (Daly, 1972).

2,4-DB [4-(2,4-Dichlorophenoxy)butyric acid]

Soybean [*Glycine max* (L.) Merr. var. Lee] and cocklebur (*Xanthium* sp.) contained β- oxidase enzymes that were capable of degrading 2,4-DB to 2,4-D. An intermediate metabolite was identified as 4-(2,4-dichlorophenoxy)crotonic acid. Another metabolic pathway was indicated by synthesis of 10-(2,4-dichlorophenoxy)decanoic acid (Wathana, 1971).

2,4-DB-^{14}C was applied to curly dock (*Rumex crispus* L.) and buckhorn plantain (*Plantago lanceolata* L.). The main pathway of metabolism was β-oxidation and 2,4-D was identified as the major metabolite. Other unidentified metabolites appeared bound to polar lipids (King, 1974).

2,4-DB methyl ester was administered in soybean oil to a guinea pig. Urine was collected and GLC-MS analysis indicated the presence of the methyl ester of 2,4-D after treatment of the extract with diazomethane (Van Peteghem and Heyndrickx, 1975).

Phytophthora megasperma var. sojae and cell suspensions of white clover (*Trifolium repens*) were not able to metabolize 2,4-D but did degrade 2,4-DB by a path not including β-oxidation (Smith and Phillips, 1976; Smith and Oswald, 1978).

Over a 21-day period, the fungus *Phytophthora megasperma* degraded about 45% of the 2,4-DB present. Since no 2,4-D was found in the nutrient medium or fungus mycelium, it was concluded that degradation did not include β-oxidation of 2,4-DB. The fungus did degrade 2,4-D (Smith and Phillips, 1976).

In Saskatchewan soils, hydrolysis of *n*-butyl 2,4-DB ester was rapid but products were not identified (Smith, 1976a).

3,5-DB [3-(3,5-Dichlorophenoxy)butyric acid]

3,5-DE [2-(3,5-Dichlorophenoxy)ethylamine]

Tomato plants were treated with 3-(3,5-dichlorophenoxybutyric acid (3,5-DB) and 2-(3,5-dichlorophenoxy)ethylamine (3,5-DE) solutions. Both compounds yielded a compound that chromatographed with a standard 3,5-dichlorophenol (Taylor and Wain, 1978).

2,4-DP [3-(2,4-Dichlorophenoxy)propionic acid]

In Saskatchewan soils, i-octyl 2,4-DP ester was rapidly hydrolyzed but products were not identified (Smith, 1976).

Susceptible and resistant plants converted 2,4-D and 2,4-DP to 2,4-dichlorophenol. Plants tested included:

- kidney bean
- soybean
- pea
- bromegrass
- wild oat
- yellow foxtail
- barley
- timothy
- orchardgrass

(Steen et al., 1974)

MCPA [4-Chloro-2-methylphenoxyacetic acid]

MCPA, labeled and non-labeled, was injected into the stomach of male rats in alcohol. Urine, feces and internal organs were analyzed. Practically all MCPA was eliminated within 5 days in urine and feces (Elo, 1976).

Roots of *Sonchus avenis* L. were injected with ^{14}C-MCPA at time of planting. Subsequent analyses revealed the presence of two components in addition to unchanged MCPA. Hydrolysis with 1N HCl or 1N NaOH yielded MCPA from the two unidentified components (Fykse, 1976).

Gloeosporium olivarum, *Gloeosporium kaki*, and *Schizophyllum commune* molds were grown in culture broths containing MCPA. Colorless needles were isolated and identified by IR spectrum, mass spectrum and elemental analysis as the ethanol analog (Nakajima et al., 1973).

MECOPROP [2-(2-Methyl-4-chlorophenoxy)propionic acid]

When mecoprop was applied to Finnish field soil, in N-Finland the $t_{1/2}$ = 20 days; and in S-Finland, $t_{1/2}$ = 4 days. After one year, forest soil in SW-Finland contained 27% of the amount found immediately after mecoprop application (Karunen et al., 1978).

2,4,5-T [2,4,5-Trichlorophenoxyacetic acid]

Sheep were fed 2,4,5-T. Analysis of muscle, fat, liver and kidney tissue showed the presence of 2,4,5-trichlorophenol (Clark et al., 1975).

2,4,5-T was administered i.v. to dogs and the plasma half-life was found to be 77 h. Studies indicated that the prolonged plasma half-life was related to urinary pH and suggested that low *in vivo* clearance was due to herbicide binding to plasma protein (Hook et al., 1976). In rats, the half-life after a single i.v. dose of 2,4,5-T was found to be dose dependent. Elimination was biphasic with a slower elimination after 84 h. The $t_{1/2}$ at 5 mg/kg was 10.7 h; at 100 mg/kg, $t_{1/2}$ = 11.0 h (0-84 h) and 69.3 h (84-168 h) (Sauerhoff et al., 1976a). When 2,4,5-T was orally administered to rats and mice, the unchanged acid was the main product in the urine. 2,4,5-Trichlorophenol and conjugates of 2,4,5-T with glycine and taurine were also observed (Grunow and Bohme, 1974).

Labeled 2,4,5-T was administered to dogfish sharks. Urine was collected and a metabolite was isolated and identified as the taurine conjugate of 2,4,5-T (Guarino et al., 1977).

Proton magnetic resonance studies indicated the 2,4,5-T binds to bovine serum albumin and that the methylene protons are closer to the binding site than the ring protons (Haque et al., 1975).

Studies with four South Vietnamese soils indicated that the soils had the capability of degrading 2,4,5-T at levels up to 15 ppm (Byast and Hance, 1975). Hydrolysis of *i*-propyl, *n*-butyl, and *i*-octyl 2,4,5-T esters in Saskatchewan soils was rapid (Smith, 1976a).

In soil, small amounts of 2,4,5-trichlorophenol were formed (Sharpee, 1973).

After incubation of soybean cotyledon callus tissue with ^{14}C-2,4,5-T for 6-15 days, water-soluble and ether-soluble metabolites were present. TLC separated the ether-soluble fraction into seven bands with only one major band present. This band was identified as a mixture of 2,4,5-T glutamate and aspartate conjugates. Chromatography and MS were used to identify these metabolites (Arjmand, 1978; Arjmand et al., 1978).

Gloeosporium olivarum, *Gloeosporium kaki*, and *Schizophyllum commune* molds were grown in culture broths containing 2,4,5-T. Colorless needles were isolated and identified by IR spectrum, mass spectrum and elemental analysis as the ethanol analog (Nakajima et al., 1973).

A mixed culture of Pseudomonas sp. and Achromobacter sp. degraded 2,4,5-T. Separately, these organisms were unable to metabolize 2,4,5-T (Sikka et al., 1976).

Combustion studies show that under normal combustion temperatures, above 500 C, destruction of 2,4,5-T esters was 99.995%. Some PCDD and PCDF may also form (Ahling et al., 1977).

Except MCPA and MCPB, phenoxyalkane carboxylic acids were only partially destroyed by ozonation in water treatment processes. Products formed included CO_2, chloride, oxalic acid, glycolic acid, and compounds with aldehydic groups (Struif et al., 1978).

2,4,5-TB [2,4,5-Trichlorophenoxy butyric acid]

4-(2,4,5-TB) was administered to a guinea pig in soybean oil. Analysis of urine extracts, using GLC-MS, indicated the presence of 2,4,5-T (Van Peteghem and Heyndrickx, 1975).

2,4,5-TP (Silvex) [2-(2,4,5-Trichlorophenoxy)propionic acid]

2,4,5-TP was ingested by seven men and one woman. Biphasic clearance from plasma and excretion in urine followed first-order kinetics. The $t_{1/2}$ for clearance from plasma was 4.0 ± 1.9 and 16.5 ± 7.3 h for initial and terminal phases, respectively. About 65% of the dose was excreted in urine within 24 h as silvex and silvex conjugates. The $t_{1/2}$ values for 2,4,5-T excretion in urine was 5.0 ± 1.8 and 25.9 ± 6.3 h for the initial and terminal phases, respectively (Sauerhoff et al., 1977b).

After 2,4,5-TP was fed to cattle and sheep, analysis of muscle, fat, liver and kidney tissues showed the presence of 2,4,5-trichlorophenol (Clark et al., 1975).

Pseudomonas sp. and Achromobacter sp. from farm pond water were unable individually to degrade 2,4,5-TP. However, when a mixed culture of these two organisms was incubated with 2,4,5-TP, extensive degradation occurred. Chlorine was released as chloride; the ring was cleaved; and CO_2 was evolved. One metabolite was identified as 2,4,5-trichlorophenol (Ou and Sikka, 1977).

4-CPA [4-Chlorophenoxyacetic acid]

In the metabolism of 4-chlorophenoxyacetic acid by enzyme preparations of *Arthrobacter* sp., 4-chlorocatechol, α-chloromuconic acid and maleylacetate were shown to be intermediates. Maleylacetate was metabolized to succinate in an NADH requiring reaction with β-ketoadipate as a probable intermediate (Tiedje, 1969).

Under sunlight or UV (300-450 nm) 4-CPA in aqueous solutions decomposed mainly to *p*-chlorophenol, phenol, hydroquinone, *p*-chlorophenyl formate, phenoxyacetic acid, *p*-hydroxyphenoxacetic acid and humic acids. In the presence of cyanide ions, irradiation of 4-CPA produced *p*-chlorobenzonitrile (Crosby and Wong, 1973).

DABDS (Dexon, Fenaminosulf) [*p*-Dimethylaminobenzenediazo sodium sulfonate]

DABDS was metabolized primarily by cometabolism in soil. The initial product was identified as *N*,*N*-dimethyl-*p*-phenylenediamine (DMPDA) (Karanth et al., 1976).

DACTHAL (Chlorthal) [Dimethyl 2,3,5,6-tetrachloroterephthalate]

Carrots treated with dacthal were analyzed for residues at harvest. In addition to unchanged dacthal, only the monoacid was observed. Residues ranged up to 0.78 ppm (Gilbert and Lisk, 1978).

Labeled chlorthal was added to pot cultures of white and Monterey pines. Within 15 days, chlorthal levels diminished by 50%. The amount of unchanged chlorthal in cultures with seedlings was 1.3-2 times greater than in fallow soils after 120 days. Degradation products were not identified (Iyer et al., 1969).

DAMINOZIDE [*N*-Dimethylaminosuccinamic acid]

Distribution and metabolism of ^{14}C-daminozide was studied in silver maple and American sycamore seedlings. Radioactivity distributed quickly after treatment and was observed in all parts of the plant. However, no metabolites were found (Domir and Brown, 1978).

DCDA (R-25788) [N,N-Diallyl-2,2-dichloroacetamide]

When fed to rats, DCDA was rapidly excreted in urine, feces, and as CO_2. Metabolites observed and identified by GC-MS included N,N-diallyl glycolamide and its glucuronide, N,N-diallyl oxamic acid, and dichloroacetic acid (Miaullis and Gray, 1974). In rats and corn plants, the major metabolites (not identified) were formed by dechlorination (Miaullis et al., 1977).

This compound and analogs have been developed as antidotes for the prevention of injury in susceptible corn species by thiocarbamate insecticides. The sulfoxide metabolites, which are presumed to be the active herbicidal compounds, were rapidly detoxified. The mechanism proposed involves increased glutathione content and glutathione S-transferase activity in the corn root. Reduction of these two compounds by thiocarbamate herbicides is then counteracted (Lay and Casida, 1976).

In soil, three of seven DCDA metabolites observed were identified as N-allyl-2,2-dichloroacetamide, N,N-diallyl-2-chloroacetamide, and N,N-diallylacetamide (Miaullis et al., 1977).

DCNB [3,4-Dichloronitrobenzene]

Genetic studies with diazinon-resistant and susceptible houseflies indicated that glutathione-dependent reactions are controlled to a high degree by genes on chromosome II. Glutathione-dependent enzyme activity was measured by using DCNB as the substrate and the change in absorbance at 344 nm was converted to nanomoles using the extinction coefficient for S-(2-chloro-4-nitrophenyl)glutathione (Motoyama et al., 1977; and Motoyama and Dauterman, 1977a and b).

DCP (DOWCO 290) [3,6-Dichloropicolinic acid]

In soil, DCP was degraded mainly by microbial activity with degradation rates greatest in moist soils. The $t_{1/2}$ was found to be about 2 months (Pik et al., 1977).

DD [Dichloropropenes plus Dichloropropane]

DD is a mixture consisting primarily of cis (or E-) and trans (or Z-) isomers of 1,3-dichloropropene and 1,2-dichloropropane. When incubated with soil, the dichloropropenes were converted to the respective 3-chloroallyl alcohols and 3-chloroacrylic acids. The latter were also obtained after hydrolysis of polar material. Dichloropropane was not appreciably degraded. No products were observed (Roberts and Stoydin, 1976c).

DDT and RELATED COMPOUNDS

DDT [2,2-Bis(*p*-chlorophenyl)-1,1,1-trichloroethane]

DDD (TDE Rhothane) [2,2-Bis(*p*-chlorophenyl)-1,1-dichloroethane]

DDE [2,2-Bis(*p*-chlorophenyl)-1,1-dichloroethylene]

KELTHANE (Dicofol) [1,1-Bis(*p*-chlorophenyl)-2,2,2-trichloroethanol]

DDT

Proton magnetic resonance showed that DDA binds with carbonic anhydrase and may be important in toxicological problems associated with DDT (Haque and Deagen, 1975). In other studies, the binding of p,p'-DDA with bovine serum albumin was demonstrated (Haque et al., 1976).

In studies with haem proteins, only the reduced forms converted DDT to DDD. Cytochrome c oxidase was active whereas cytochrome c itself was inactive, indicating that an accessible haem site is necessary for the reaction (Stotter et al., 1977).

DDT was incubated with hematin, blood and sewage sludge. Compounds were identified by comparison of their MS spectra with those of standards. Sodium dithionite was included in the incubations to reduce Fe^{+3} porphyrins to Fe^{+2} porphyrins; aqueous sodium carbonate, to dissolve hematin; and NH_3 in some incubations, to be a source of nitrogen for such products as DDCN. Results are summarized in the following table (Marei et al., 1978).

DDT Degradation

Incubation mixture	Metabolites					
	DDD	DDE	DDMU	DDA	DBP	DDCN
NH_3	ND	ND	ND	+	ND	ND
Hematin	+++	++	+	+++++	+	ND
Hematin + NH_3	+++++	+	+	++	+	++
Fresh blood	++++	+	+	+++	+	ND
Fresh blood + NH_3	++++	+	+	+++	++	+
Heated blood	+++++	+	+	++++	+	ND
Heated blood + NH_3	++++	+	+	+++	+	+
Sewage sludge	+++++	+	+	++	+	+
Sewage sludge + NH_3	+++++	+	+	+++	+	+
Sewage sludge + Fresh blood	+++++	+	+	+++	+	+
Sewage sludge + Fresh blood + NH_3	++++	+	+	+++	+	+
Sewage sludge + Heated blood	++++	+	+	+++	+	+
Sewage sludge + Heated blood + NH_3	++++	+	+	+++	+	+

When fed to Pennsylvania white-tail deer, p,p'-DDT was metabolized mainly to p,p'-DDD. Small amounts of p,p'-DDE also formed (Kurtz and George, 1976).

After white male rats were orally administered ^{14}C-ring-labeled DDT, $^{14}CO_2$ as well as feces and urine were collected. The studies showed that a small amount of DDT underwent ring oxidation; that most radioactivity was excreted in the feces; and that the level of ^{14}C excreted as $^{14}CO_2$ was equal to the ^{14}C excreted in the urine (Abou-Donia and Menzel, 1976).

^{14}C-*p,p*'-DDT in olive oil was administered to CF-1 mice and Syrian golden hamsters by gavage. Urine was collected and analyzed by TLC and autoradiography. In both mouse and hamster, DDA and DDA conjugates were observed. In addition to a glucuronic acid conjugate, glycine, alanine, and serine conjugates were identified. Three other compounds were not present in sufficient quantity for identification. Both animals excreted DDD, DBP, and DDOH, but larger amounts were observed in mouse urine. Noticeable because of its absence, no DDE was ever observed in the hamster urine in replicate experiments. Small but significant amounts of DDE were observed in mouse urine (Gingell, 1976).

Female rats were dosed orally with ^{14}C-ring-labeled *p,p*'-DDT during pregnancy or lactation. Clearance of DDT in milk decreased with a rate constant of -0.096 and $t_{1/2}$=7.2 days. DDD and DDE increased in neonate liver as DDT decreased. Average $t_{1/2}$=10.6 h in tissues and fetus. Metabolism of DDT was more rapid in the adult liver than in the neonate liver. While DDA was observed, it was not present in all tissues (Fang et al., 1977).

When technical DDT was added to rations of sheep (250 ppm *p,p*'-DDT), a plateau at 524 ppm *p,p*'-DDT, 75 ppm *p,p*'-DDD and 25 ppm *p,p*'-DDE in subcutaneous fat was reached in 8 weeks. The computed depletion $t_{1/2}$ was 90, 26 and 223 days, respectively (Reynolds et al., 1976).

GC and mass spectral analyses conducted with fat samples from the Baltic grey seal (*Halichoerus grypus*), ringed seal (*Pusa hispida*) and common seal (*Phoca vitulina*) indicated the presence of the *o*- and *m*-methyl sulfones of DDE. Other sulfones were also present. American mink (*Mustela vison*) were fed DDT and DDE at levels found in Baltic herring, the main food of the seal. Analysis of fat showed the presence of methyl sulfones of DDE and a pattern similar to that found in seals (Jensen and Jansson, 1976).

In vitro studies with mid- and hind-gut contents of young hatchery-reared Atlantic salmon converted *p,p*'-DDT to *p,p*'-DDD (Cherrington et al., 1969). In other studies with Atlantic salmon parr, DDT was degraded to DDD and DDE (Greer and Paim, 1968).

In trout *p,p*'-DDT was metabolized to DDE, DDD, and DDMU. DDMU was apparently the final degradation product of DDT in trout. However, the conversion rate of DDT to DDD to DDMU was one-tenth the rate of DDT conversion to DDE. Consequently, DDE accumulates most (Addison, 1978).

In other studies, rainbow trout (Salmo gairdneri) were injected with ^{14}C-labeled p,p'-DDT and its metabolites. Water and tissues were analyzed. Results are summarized:

Compound	Metabolite(s)
p,p'-DDT	p,p'-DDE; p,p'-DDD
p,p'-DDE	(not degraded)
p,p'-DDD	p,p'-DDMU
p,p'-DDMS	p,p'-DDNU
p,p'-DDNU	(not degraded)
p,p'-DDMU	(not degraded)
p,p'-DDOH	p,p'-DBP
p,p'-DBP	limited interconversion with DBH
p,p'-DBH	limited interconversion with DBP
p,p'-DDA	p,p'-DBP

(Addison and Willis, 1978)

When brook trout (Salvelinus fontinalis) were intramuscularly injected with p,p'-[^{14}C]DDT, DDD and DDE were formed. Further conversion of DDD to DDMU was very slow (<1% in 5 weeks) and no further metabolism of DDE or DDMU was observed under the conditions of the experiment (Addison and Zinck, 1974). In other studies, the rate of production of DDE varied with temperature (Zinck and Addison,, 1975). Pretreatment of brook trout with injections of p,p'-DDT, p,p'-DDE, p,p'-DDD or p,p'-DDMU did not influence the rate of dehydrochlorination (Addison and Zinck, 1977).

Winter flounder converted DDT, injected via the caudal vein, to DDD, DDE and unidentified polar metabolites (Pritchard, 1972). In addition to these two metabolites, two dimensional chromatography demonstrated compounds behaving similarly to DDA and DBP. In winter flounder caught for background purposes, DDMU, the p,p'-isomers of DDT, DDD and DDE, and o,p'-DDD and o,p'-DDT were found (Pritchard et al., 1973).

Atlantic salmon (Salmo salar) fry were injected intramuscularly with tritiated p,p'-DDT. About 60% of the material remained after 8 weeks. DDT conversion to DDE exhibited a $t_{1/2}$ of 60 days (Addison et al., 1976).

Mosquito fish (Gambusia affinis) metabolized p,p'-DDT to p,p'-DDD and p,p'-DDE. DDE was the major metabolite (Pillai et al., 1977b).

The uptake rate from food and the biological half-life of DDT for young-of-the-year menhaden was calculated at several DDT levels.

Dose Level (ppb)	$T_{1/2}$ (days)
0.58	428
9.0	64
93.0	137

The linear DDT flux model was $FD_{f}a = (\gamma + \lambda)\ (D_m)$

where F = daily feeding rate
D_f = concentration of DDT in food
a = fraction ingested DDT that is assimilated
γ = daily fractional DDT accumulation rate
λ = daily fractional turnover rate
D_m = DDT concentration in menhaden

(Warlen et al., 1977).

The freshwater snail *Vivipara heliciformis* metabolized DDT to DDD and DDE. Snails exposed to DDT accumulated this compound to high levels but also excreted it rapidly when placed in an aquarium containing fresh pond water (Yadav et al., 1978).

When marine copepods (*Calanus* spp.) were exposed to about 450 pptr *p*,*p*'-DDT, an equilibrium level of 50-100 ppm (dry wgt) was reached after 3-4 weeks. No metabolites were detected (Darrow and Harding, 1975). Because uptake and depuration occur simultaneously in copepods, measurement of the uptake rate was very difficult. Calculations indicated that copepods lose *p*,*p*'-DDT in flowing sea water with a rate constant of k =0.048/day; uptake is described by

$$\frac{dC}{dt} = k_i \frac{\mu}{a} W - k_j C, \text{ where}$$

k_i varied between 1.5 and $2.7\text{x}10^3$/day (Harding and Vass, 1977).

Freshwater invertebrates were placed in continuous-flow apparatus and [^{14}C]-*p*,*p*'-DDT was added. Degradation of DDT is summarized.

Organism	Metabolite(s)
Cladocera (*Daphnia Magna*) - mature adult	DDE, DDD
Amphioda (*Gammarus fasciatus*) - mature adult	DDE
Decapoda (*Palaemonetes kadiakensis*) - mature adult	DDE, DDD, Kelthane, DBP
Ephemeroptera (*Hexagenia bilineata*) - nymph	DDE

Odonata (*Ischnura verticalis*) - naiad	DDE
(*Libellula* sp.) - naiad	DDE, Kelthane
Diptera (*Chironomus* sp.) - larvae	DDE

(Johnson et al., 1971)

In surface seawater at 4 to 32C, no degradation of DDT was observed. When *Cylindrospermum* sp. cells were added, DDT formed. With addition of organic amendments also, DDD and DDE were produced. Flooded sediments were very active in degrading DDT to DDD. An unidentified compound accumulated in the sediments (Juengst and Alexander, 1975).

In the preparation of an alcoholic drink from grapes, DDT was degraded to DDD during the fermentation (Kawar and Dagher, 1976). Ensilage and field drying effected no significant decrease in the contents of *p,p*'-DDT, *p,p*'-DDD, *p,p*'-DDE and *o,p*'-DDT on grass and alfalfa (Smelt et al., 1975).

After cotton was sprayed with DDT, seeds from the first pick contained *p,p*'-DDT and *p,p*'-DDE (El Zorgani, 1975).

Although DDT absorption rates in three strains of housefly showed no diel rhythm, the rate of DDT breakdown to DDE did show a diel rhythm with most rapid breakdown at 05:00 to 05:30 and 15:00 h. This corresponds to diel peaks in oxygen consumption (Shipp and Otton, 1976).

p,p'-DDT, fed to larvae of gypsy moth, was metabolized into the three major metabolites DBH, DDD and DDE. DDA and DBP were metabolized primarily to DBH; DDE and DDD were metabolized in part to DBH. DBH was not further metabolized by gypsy moth larvae. Small amounts of dicofol were observed (Respicio, 1976).

DDT degradation in water was determined at pH's observed in the environment and at 27C.

	$t_{1/2}$	
	pH 9	pH 5
DDT	81 days	12 yr
DDD	570	190
DDMS	3400	1200
DDE	(-HCl)	>120

(Wolfe et al., 1976c and 1977b).

Studies of DDT conversion to DDE in soil indicated that it was predominantly a chemical process (Guenzi and Beard, 1976a). When DDT ws incubated with Raber silt loam under flooded (anaerobic) conditions, DDT was degraded to DDE and DDD. Further degradation of DDD to DDMU was observed and found to be temperature dependent (Guenzi and Beard, 1976b).

Residues of DDT in a subtropical soil consisted of *p,p*'-DDE, DDD, and DDA in addition to unchanged DDT (Talekar et al., 1977b).

Forty-seven of 110 bacteria isolated from seawater and marine sediment converted up to 10% of supplied DDT into water-soluble products. When *Mucor alternans* was incubated with DDT, three compounds distinct from known DDT metabolites were produced. None were identified (Juengst and Alexander, 1976).

Cultures of the soil amoeba *Acanthamoeba castellanii*, incubated with DDT, produced DDE, DDD and DBP. TLC and GLC were used to identify these metabolites. Some chromatograms exhibited peaks with retention times corresponding to DDOH and DDMU but this could not be confirmed (Pollero and de Pollero, 1978).

The earthworm *Pheretima posthuma* metabolized *p,p*'-DDT to *p,p*'-DDE and *p,p*'-DDD rapidly. Within 24 h, about 35% of the DDT was metabolized (Agarwal et al., 1978).

A study was undertaken to study the fate of DDT in a forest liter macro-arthropod food chain. Collembola were fed *o,p*'-DDT, *p,p*'-DDT or *p,p*'-DDE and then released into the field. Over a period of a few days, *p,p*'-DDT was degraded below 0.01 ppm and only *p,p*'-DDE was detected. The most rapid converters of p,p'-DDT among the arthropod cryptozoan predators were Thomisidae, Elateridae larvae, Carabidae, and Staphylinidae. Formation of *o,p*'-DDE started almost immediately after feeding on *o,p*'-DDT-fed Collembola. In this study, the conversion of *o,p*'-DDT to *p,p*'-DDT and *p,p*'-DDE is reported. (Previous accounts of such a conversion have been subsequently accounted for by the presence of small amounts of *p,p*'-DDT in the *o,p*'-DDT. This possibility was not addressed.) *p,p*'-DDD was also observed as a metabolite of *p,p*'-DDT. When *p,p*'-DDE was used, no identifiable metabolites were found (Manley et al., 1976). In another study, when DDT was applied to a forest, the data indicated that the decay of DDT residues in northern Maine soils could approximate the 35-year half-life suggested by others (Owen et al., 1977).

Studies were conducted with *Pseudomonas putida*, an organism capable of using diphenylmethane and benzhydrol as sole carbon sources. By cometabolism, bis(*p*-chlorophenyl)methane (DDM) was metabolized with formation of *p,p*'-dichlorobenzhydrol (DBH), *p,p*'-dichlorobenzophenone (DBP), benzhydrol (BH), benzophenone (BP), *p*-chlorophenylacetic acid

(PCPA), and *p*-chlorophenylglycolaldehyde (PCPG). When dichlorobenzhydrol was incubated with this organism, BH and BP formed. Cometabolism of DDA produced DDM, DBH, and DBP. DBP was not further degraded when incubated with this bacterium (Subba-Rao and Alexander, 1977a).

In other studies with *Pseudomonas putida*, incubation with the DDT analog diphenylmethane as a sole carbon source produced 1,1,1',1'-tetraphenyldimethyl ether (TPDE). GC, MS, IR, and NMR were used to identify this compound and others formed: BP, BH, phenylglycolic acid, and phenylacetic acid. When BH was incubated with resting cells, phenylglycolic acid, a hydroxy-BP, and compounds that appear to be hydroxybenzhydrols were formed. TPDE was also converted to BH and BP (Subba-Rao and Alexander, 1977b).

When an *Arthrobacter* sp. was incubated with *p*-chlorophenylacetate, GC-MS was used to identify one of two products as 4-chloro-3-hydroxyphenylacetate (Deo and Alexander, 1976).

UV irradiation of *p,p*'-DDT in a reactor produced DDE primarily with smaller amounts of DDD and other compounds. DDE yielded DDMU and DCB primarily and seven other products identified as dichlorobiphenyl, a DCB isomer, trichlorobiphenyl, a DDMU isomer, tetrachlorobiphenyl, a DDE isomer, and a compound only identified as $C_{12}H_6Cl_2O$. In those studies where a reflector was used in conjunction with the reactor, 3,6-dichlorofluorenone also formed from *p,p*'-DDE (Crosby and Moilanen, 1977).

Addition of diphenylamine and diethylamine to commercial DDT formulations enhanced photodegradation of DDT when sprayed on plants (Parmar et al., 1976).

Aromatic amines were reacted with DDT analogs. When methoxy (I) or ethoxy (II) compounds were heated to boiling with $4-CH_3$- or 4-Cl dimethylaniline, the corresponding ethylene analog (III) was formed as well as the dichloroethane (IV) and monochloroethylene (V) analogs. Upon prolonged heating, compound IV was converted to dialkoxystilbenes (VII) and dialkoxydiphenylethyenes (VIII). When 1,1-bis(*p*-methylphenyl)-2,2,2-trichloroethane (IX) was used, the corresponding dichloroethylene (X), dichloroethane (XI), and stilbene (XII) formed. DDT itself formed only the stilbene and dichloroethylene. When 4-Br-dimethylaniline was used, the DDT analogs yielded the corresponding dichloroethylenes, as well as secondary and tertiary basic compounds (Baghos et al., 1977a and b).

p,p'-DDT was incubated with hydroxycob(III)alamin at pH 7.4. Reduction of DDT to DDD occurred in light or dark conditions (Berry and Stotter, 1977).

Studies on disposal of DDT showed that, when powdered zinc, acetone and acetic acid were mixed with DDT and soil at time of burial, DDD and DDMS formed. DDE present at time of burial was not appreciably affected and none was formed. o,p'-DDT and o,p'-DDE gave similar results (Staiff et al., 1977).

When DDT was heated to boiling with dimethylaniline, β-elimination gave DDE. Secondary and tertiary compounds were also obtained (Tadros et al., 1976).

Patients under treatment with o,p'-DDD for adrenocortical carcinoma also excreted o,p'-DDA and a conjugate in the urine (Sinsheimer et al., 1972).

In other studies, urine from patients being treated with o,p'-DDT for adrenal cortical carcinoma was collected and analyzed. Ether extracts were methylated and examined by GLC-mass spectroscopy. Five metabolites were detected and identified using the GLC renention times, mass spectra, and IR spectra. Identified as methyl derivatives were o,p'-dichlorodiphenylacetate (o,p'-DDA); 1-(2-chloro-4-hydroxyphenyl-1-(4-chlorophenyl)acetate; 1-(2-chloro-3-hydroxyphenyl)-1-(4-chlorophenyl)acetate; 1-(2-chloro-3,4-dihydroxyphenyl)-1-(4-chlorophenyl)acetate; and o,p'-dichlorodiphenylacetylglycine. The 4,5-dihydroxy- and 5-hydroxy- analogs of o,p'-DDA were observed by GLC only (Reif et al., 1974).

Rabbits fed o,p'-DDD for 11-18 days excreted o,p'-DDA in urine (Sinsheimer et al., 1972).

^{14}C-o,p'-DDD was incubated with adrenal fractions from dog. Thin-layer chromatography and autoradiography showed that the adrenal mitochondria metabolized the DDD to five polar metabolites. Only o,p'-DDA identity was established and confirmed by mass spectrometry. Other unextractable compounds also were apparently formed and bound to macromolecules. NADPH was required but CO or heating mitochondria inhibited the metabolism (Martz and Straw, 1977).

Two laying Japanese quail hens were exposed to ^{14}C-DDE. Eggs, excretory matter, brain liver and carcasses were analyzed. No metabolites of DDE were observed (Lamberton et al., 1975).

DDD residues in livers of pigeons, Bengalese finches and Japanese quail, which were dosed with pure p,p'-DDT, were always low immediately after death. Postmortem reductive chlorination occurred rapidly at 20C and was apparently the result of anaerobic processes within the cell. Reductive chlorination occurred in brain and in embryos but not significantly in depot fat or in eggs without embryos (Walker and Jefferies, 1978).

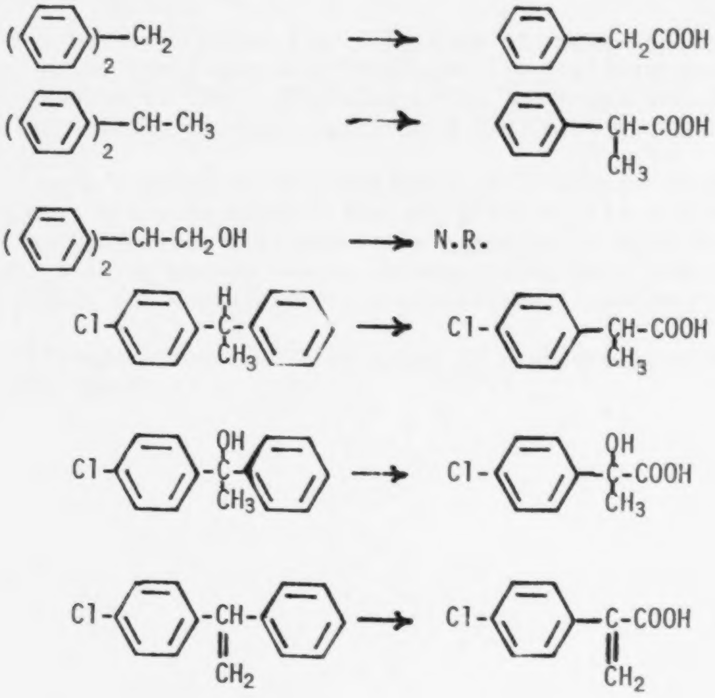
Rats were fed *p,p*'-DDE in peanut oil and feces were collected for one week. GC and mass spectral comparison with synthesized compounds revealed the presence of 3-HO-DDE (II), thee major metabolite, and three minor metabolites: 4-HO-DDE (III), 2-HO-DDE (IV), and 1,1-dichloro-2-(4-hydroxyphenyl)-2-(4-chlorophenyl)ethylene (V) (Sundstrom, 1977).

An active photosensitizer, that promoted DDT degradation, was obtained from a heat denatured algal [*Anacystis nudilans* (TX20)] preparation. This was identified as small molecular weight flavoproteins that appear to act as proton donors in the presence of flavin cofactors. The product of this reducing system was DDD. This was also observed with fresh water blue-green algae [*Microcystis aeruginosa* (Indiana 1036)] (Matsumura, 1978). A low molecular weight flavoprotein, isolated from rat intestinal wall, also was found capable of dechlorinating DDT to DDD. The flavoprotein apparently converted FAD to FADH which actually reacted with DDT to produce the DDD (Esaac and Matsumura, 1977).

Photolysis of DDT plus diethylaniline in methanol in air produced 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethane, 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene, 4,4'-dichlorobenzophenone, methyl 1,1-bis(*p*-chlorophenyl)acetate, α,α-bis(*p*-chlorophenyl)-*p*-diethylamino acetophenone, and diethylaniline hydrochloride as the major products; *cis*- and *trans*-1,1,4,4-tetrakis(*p*-chlorophenyl)-2-butene, 1,1-bis(*p*-chlorophenyl)-2-*p*-diethylaminophenyl)-2-methoxy ethylene, 1,1-bis(*p*-chlorophenyl)-2,2-bis(*p*-diethylaminophenyl)ethylene as the minor products (Narang, 1972).

Photolysis of DDE in water, benzene, and hexane produced *o*-Cl-DDMU in about 20% yield. Dichlorobenzophenone was also formed in 15% yield. In benzene no DDMU formed. Very little formed in water. In hexane, degassing dropped the yield of dichlorobenzophenone (DCB) to zero but increased DDMU yield to 56%. Photolytic half-lives calculated for dissolved DDE near the surface of a body of water at latitude 40°N were spring 1.4 days, summer 0.94 days, fall 2.4 days, and winter 6.1 days (Zepp et al., 1977).

A *Pseudomonas* sp. was isolated from sewage and found capable of metabolizing 1,1-diphenylethane as its sole source of carbon. This organism was able to metabolize mono-*p*-chlorophenyl analogs of DDT but not the *p,p*'-dichlorophenyl analogs as sole carbon sources. Those chlorinated acids formed were not further metabolized (Francis et al., 1976). When diphenylethane (DPE) was added to the culture medium, bis(*p*-chlorophenyl)methane and 1,1-bis(*p*-chlorophenyl)ethane were metabolized to produce *p*-chlorophenylacetic acid and 2-(*p*-chlorophenyl) propionic acid. These were not further degraded by this bacterium. During the initial phase of incubation, two other metabolites were observed. Mass spectra data indicated that these transitory compounds were 1-(4-chloro-2-hydroxyphenyl)-1-(4-chlorophenyl)ethane and 1-(4-chloro-3-hydroxyphenyl)-1-(4-chlorophenyl)ethane. Cometabolism of 1,1-bis(p-chlorophenyl)ethene or 1,1-bis(p-chlorophenyl)-2-chloroethene with DPE produced 2-phenylpropionic acid, which was converted to 2-phenyllactic acid (Francis et al., 1978).


CH2
CH2COOH
CH-CH3
CH-COOH
CH3
CH-CH2OH
N.R.
Cl
H
C
CH3
CH-COOH
CH3
OH
C
CH3
OH
C-COOH
CH3
CH
CH2
C-COOH
CH2

(Francis et al., 1976)

Catalytic dechlorination of DDT with nickel boride produced mixtures of III, IV, V, VI, VII and VIII.

(Dennis and Cooper, 1975)

In CH_2Cl_2-CH_2OH, tetraphenylporphyrin (II) [TTP-Fe^{+2}] was reacted with DDT and an excess of iron powder. A complex that was formed was identified as a TTP-Fe^{+2} vinylidene carbene complex and in agreement with those of a pentacoordinated TTP-Fe^{+2} complex with the $C{=}C(C_6H_4Cl)_2$ ligand (Mansuy et al., 1978).

DDVP (Dichlorvos) [O,O-Dimethyl O-(2,2-dichlorovinyl)phosphate]

After administration of DDVP to rats, analysis of collected urine indicated the presence of O,O-dimethyl phosphoric acid (Bradway et al., 1977).

After inhalation by or i.p. injection of $^{14}CH_3$-labeled DDVP into mice, urine contained methyl-labeled 7-methylguanine. When *E. coli* were exposed to DDVP containing $^{14}CH_3$, both RNA and DNA contained labeled 7-methylguanine (Wennerberg and Lofroth, 1974).

Swine were exposed to an atmosphere of [1-vinyl-^{14}C]dichlorvos for 24 days. Analyses showed labeling primarily in glycine and serine. Glycine conversion followed known pathways to adenine and nucleic acids. Serine metabolism to carbohydrates gave some labeled glucose and ribose and acetate-derived cholesterol (Loeffler et al., 1976).

In oil preparations, DDVP degraded to dichloroacetaldehyde at 70C to 150C (Ogato et al., 1976).

DEMETON (Systox, Bayer 19639)

Isosystox or Demeton S:Methyl isosystox is O,O-dimethyl S-ethyl-2-thioethyl phosphorothiolate

Plants converted methyl isosystox to the sulfoxide and sulfone. Hydrolysis within the plant initially gave dimethyl phosphoric acid and then inorganic phosphate. Some phosphorus is incorporated into the plant materials. Methyl isosystox sulfoxide ingested by animals is quickly eliminated (Tietz, 1960).

DENMERT S-1358 [S-*n*-Butyl S'-*p*-*tert*-butylbenzyl *N*-3-pyridyldithiocarbonimidate]

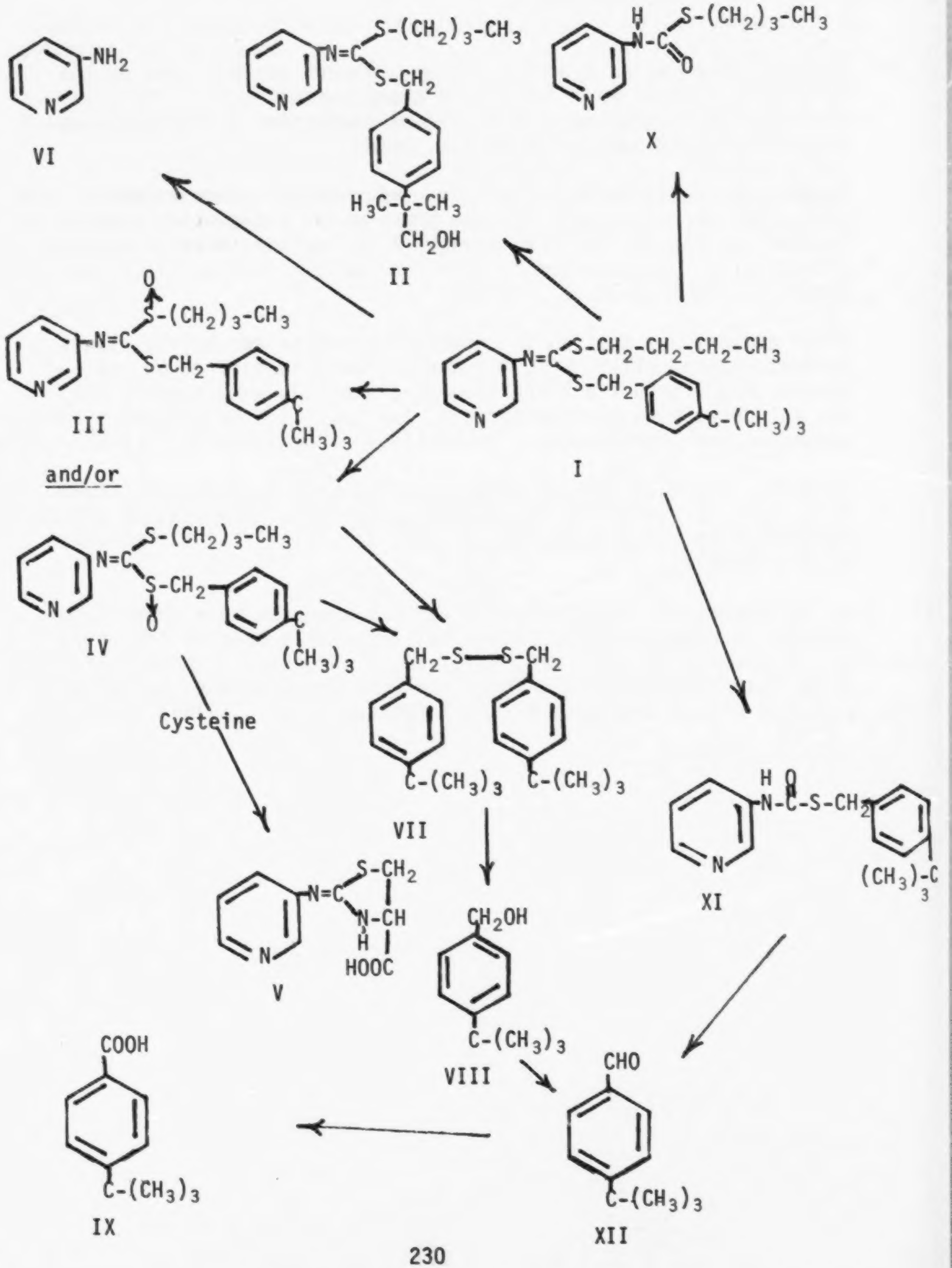
In a rat liver mixed function system, denmert was oxidized to two isomers of sulfoxides. These were transient metabolites *in vivo* and were metabolized to a thiazolidine derivative in the presence of ℓ-cysteine (Miyamoto and Ohkawa, 1978).

Denmert was incubated with rat liver microsomes. Both isomeric sulfoxides were observed. In the presence of l-cysteine, both reacted non-enzymatically to produce 2-(3'-pyridylimino)-4-carboxylthiazolidine. In addition to this, compounds II-IV and VI-IX were identified (Ohkawa et al., 1976a).

After denmert was applied to cucumber, snapbean and barley plants, denmert S-oxide (III), VII, XI, and XII were identified on leaf surface and within the leaf. Some β-glucosides were present but the aglycones were not identified. The half-life in cucumbers and snapbeans was 3 and 2 weeks, respectively (Ohkawa et al., 1976b).

In soils, the half-life of denmert varied from 3 months in Katano sandy loam to 1 month in Utsunomiya silty loam. Degradation products identified included compounds II, III, VII, VIII, IX, XII (Ohkawa et al., 1976b).

On TLC plates, UV irradiation of denmert produced more than 10 compounds. Chromatography and chemical tests were used to identify six of these: III, VI, VII, VIII, IX, X, XI, XII. Exposure of denmert on TLC plates to natural sunlight produced the same photoproducts except compounds VI and X (Ohkawa et al., 1976b).

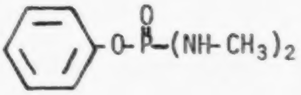

VI
II
X
III
and/or
I
IV
Cysteine
VII
XI
V
VIII
IX
XII

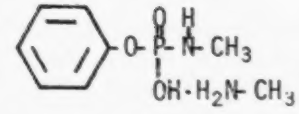
DIAMIDFOS (Nellite) [*N*,*N*'-Dimethylphenylphosphorodiamidate]

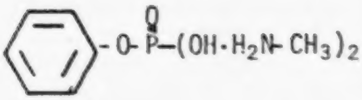
After i.v. administration of ^{14}C-diamidfos to rats, plasma clearance was found to be first-order with a half-life of about 3 h. Metabolites eliminated in urine were identified by GC-MS, IR, and NMR spectrometry as phenol, *N*-methylphosphorodiamidate, and *N*-formyl-*N*'-methylphosphorodiamidiate (Sauerhoff et al., 1976).

When tobacco was treated with ^{14}C-diamidfos, in addition to unchanged diamidfos and unextractable material, phenyl β-D-glucopyranoside and a glycoside of phenol were observed. In tobacco smoke, the major breakdown product was phenol (Meikle, 1977).

Diamidfos hydrolysis did not occur in phosphate buffer (pH 7.1) or in borate buffer (pH 7.9). Acid hydrolysis produced *N*-methyl hydrogen phosphoroamidate, dihydrogenphenyl phosphate and methylamine (Meikle, 1978).







DIAZINON [O,O-Diethyl O-(2-isopropyl-4-methyl-6-pyrimidinyl)phosphorothioate]

Hepatic microsomal preparations and liver slices were made from sheep, cow, pig, guinea pig, rat, turkey, chicken and duck. Metabolism of diazinon with these preparations is tabulated.

Species		Metabolites	
		Microsomes	Liver slices
Sheep	lamb	I-V	
	adult	I-VI	I-V
Cow		I-VI, VIII	
Pig	male	I-VI, VIII	I-V, VIII
Guinea pig	male	I-VI	I, III, IV
Rat	male	I-VII	I-V
Turkey	male	I-VIII	I-IV
Chicken	female	VI	I-VI
Duck	young male	I-VI, VIII	

(Machin et al., 1975)

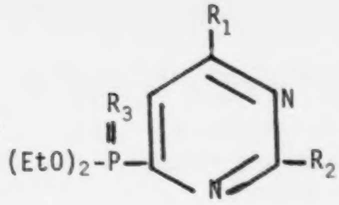
Diazoxon was incubated with plasma from sheep, cow, pig, rabbit, rat, guinea-pig, turkey, chicken and duck. Mammalian plasmas--rabbit and sheep--showed greatest activity, poultry, lowest activity. Diazoxon was enzymatically hydrolyzed in sheep plasma with liberation of pyrimidinol. The half-life of diazoxon in plasma varied from a few seconds in sheep to several hours or longer in chicken and turkey (Machin et al., 1978).

Rat liver glutathione S-transferases were separated on a hydroxyapatite column and numbered I-IV as they eluted. Incubation of diazinon with transferase III and IV produced S-(2-isopropyl-4-methyl-6-pyrimidinyl) glutathione and diethyl phosphorothioic acid (Usui et al., 1977).

Diazinon was incubated with a GSH S-aryltransferase prepared from fly homogenates. Three metabolites were observed with TLC. Co-chromatography was used to identify two metabolites as desethyl diazinon and S-(2-isopropyl-4-methyl-6-pyrimidinyl)glutathione (Motoyama and Dauterman, 1975).

Enzyme preparations from corn, soybeans, and lima beans degraded diazinon and produced primarily 2-isopropyl-4-methyl-6-hydroxypyrimidine (Ioannu, 1978).

Diazinon was applied to leaves of bean plants (Phaseolus vulgaris L.). Translocation was rapid. Large decreases in foliar residues were probably the result of hydrolysis of P-pyrimidinyl bond. Only diazinon was recovered (Finlayson et al., 1976b).



	R_1	R_2	R_3
Diazinon	CH_3	$CH-(CH_3)_2$	S
I	CH_3	$-\underset{CH_3}{\overset{OH}{C}}-CH_3$	S
II	CH_2OH	$-\overset{CH_3}{CH}-CH_3$	S
III	CH_3	$-\overset{CH_3}{C}=CH_2$	S
IV	CH_3	$-\overset{CH_3}{CH}-CH_3$	0
V	CH_3	$-\underset{CH_3}{\overset{OH}{C}}-CH_3$	0
VI	CH_2OH	$-\overset{CH_3}{CH}-CH_3$	0
VII	CH_3	$-\overset{CH_3}{C}=CH_2$	0
VIII	CHO	$-\overset{CH_3}{CH}-CH_3$	S

DICAMBA [3,6-Dichloro-*o*-anisic acid]

VEL-4207 [(Phenylimino)diethylene bis(3,6-dichloro-*o*-anisate)]

^{14}C-Labeled dicamba was applied to western bracken (*Pteridium aquilinum* (L.) Kuhn var. pubescens Underw.). Analyses indicated that dicamba was translocated to rhizome apices and metabolized to 5-hydroxy-3,6-dichloro-*o*-anisic acid and 3,6-dichlorogentisic acid (Robocker and Zamora, 1976).

When ^{14}C-dicamba was added to a model ecosystem, radioactivity was found throughout the system. Decarboxylation occurred very slowly. Most of the herbicide and its metabolites were conjugated or in anionic form. In addition to dicamba, 5-hydroxydicamba and conjugated products were present. In the crab extract, there was no dicamba or detectable 5-hydroxydicamba. Hydrolysis of crab extracts, however, contained 5-hydroxydicamba, indicating the presence of conjugated products in the crab (Yu et al., 1975c).

Under field conditions, dicamba and VEL-4207 both yielded 3,4-dichlorosalicylic acid. When VEL-4207 was used, dicamba was also observed. After 16 weeks, 16% of the dicamba and 60% of the VEL-4207 applied remained in the top 7.5 cm of soil. The *N*-phenyldiethanolamine moiety was bound in the soil or converted to CO_2 (Harger, 1976; Harger and Rieck, 1976). In extracts of sand and worms from plots treated with dicamba, in addition to unchanged dicamba, two metabolites found in the sand extracts were identified as 3,6-dichlorosalicylic acid and 5-hydroxy dicamba. The latter was also found in the worm extracts (Chio and Sanborn, 1978).

DICHLOBENIL [2,6-Dichlorobenzonitrile]

Dichlobenil was applied to aquatic plants. When dichlobenil was applied to water cress (Rorippa nasturtium-aquaticum L. Hayek), chromatography indicated the presence of the 3-OH and 4-OH analogs in roots and 2,6-dichlorobenzamide (2,6-BAM) in the stems. The 3-OH and 4-OH compounds seemed to be present in stems and roots of narrow-leafed water parsnip (Berula erecta Huds. Coville) and 2,6-BAM possibly present in B. erecta leaves. The 3-OH and 4-OH metabolites were present in all regions of reedgrass (Phragmites communis Trin.) (Mottley and Kirkwood, 1978).

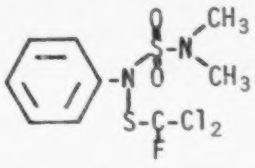
DICHLOFENTHION [*O*,*O*-Diethyl *O*-(2,4-dichlorophenyl)phosphorothioate]

After male Sprague-Dawley rats were exposed to dichlofenthion, analysis of urine indicated the presence of *O*,*O*-diethyl phosphoric acid, *O*,*O*-diethyl phosphorothioic acid, and 2,4-dichlorophenol (Bradway et al., 1977).

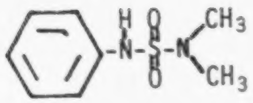
DICHLOFLUANID (Euparen) [N'-Dichlorofluoromethylthio-N,N-dimethyl-N'-phenylsulfamide]

When applied to strawberries, dichlofluanid disappearance followed first-order kinetics in the first 21 days (Seifert et al., 1978).

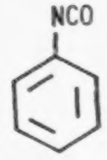
In methanol, benzene, and acetone, dichlofluanid (I) was degraded by UV. After irradiation in acetone, the following products were identified: N,N-dimethyl-N'-phenylsulfamide (II), phenyl isocyanate (III), phenyl isothiocyanate (IV), bis(dichlorofluoromethyl)disulfide (V), dimethylamidosulfonyl chloride (VI), 1-(dichlorofluoromethylthio)propan-2-one (VII), and 1-(dichlorofluoromethylsulfonyl)propan-2-one (VIII) (Clark and Watkins, 1978).



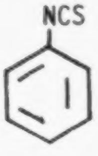
I



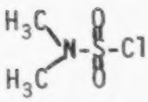
II



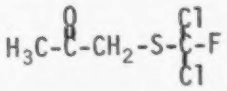
III



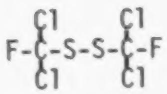
IV



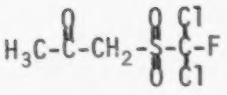
VI



VII



VIII



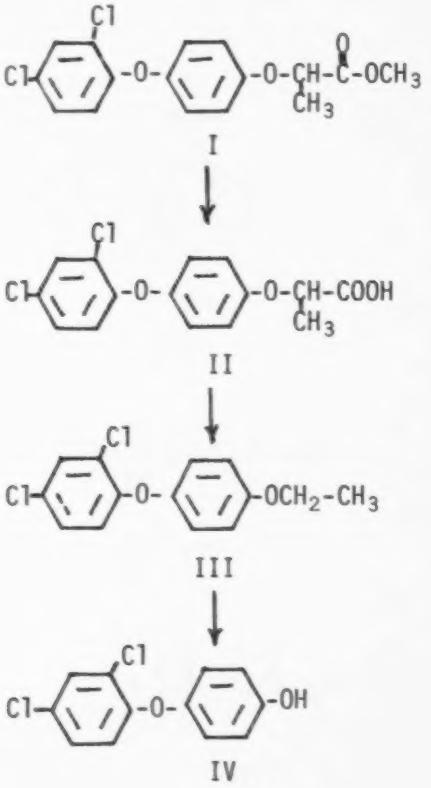
VIII

DICHLORFOP-METHYL (Dichlofop-methyl; HOE 23408 OH) [(±)-Methyl 2-[4-(2,4-dichlorophenoxy)phenoxy]propionate]

This herbicide was applied to wheat at the rate of 1 kg/ha. Analyses of plant material indicated the presence of unchanged herbicide in addition to a number of metabolites. The main metabolites were identified with GC-MS as the free acid (II), 5'-OH-analog, and 3'-OH- and 6'-OH-analogs of the free acid as plant conjugates (Gorbach et al., 1977).

The breakdown of dichlorfop-methyl in moist nonsterile clays and sandy loam was investigated. Rapid hydrolysis to the acid (II) occurred initially. This bound tightly to the soils. Subsequently, there was decarboxylation to the ethyl analog (III) and cleavage of the ethyl moiety to produce 2,4-dichlorophenoxy-p-phenol (Smith, 1976b and 1977).

In soils, dichlofop-methyl ester bond was rapidly hydrolyzed and the substituted propionic acid was aerobicly oxidized to CO_2. An intermediate was identified as 4-(2,4-dichlorophenoxy)phenol. Under anaerobic conditions, only a small degree of degradation occurred (Martens, 1978).

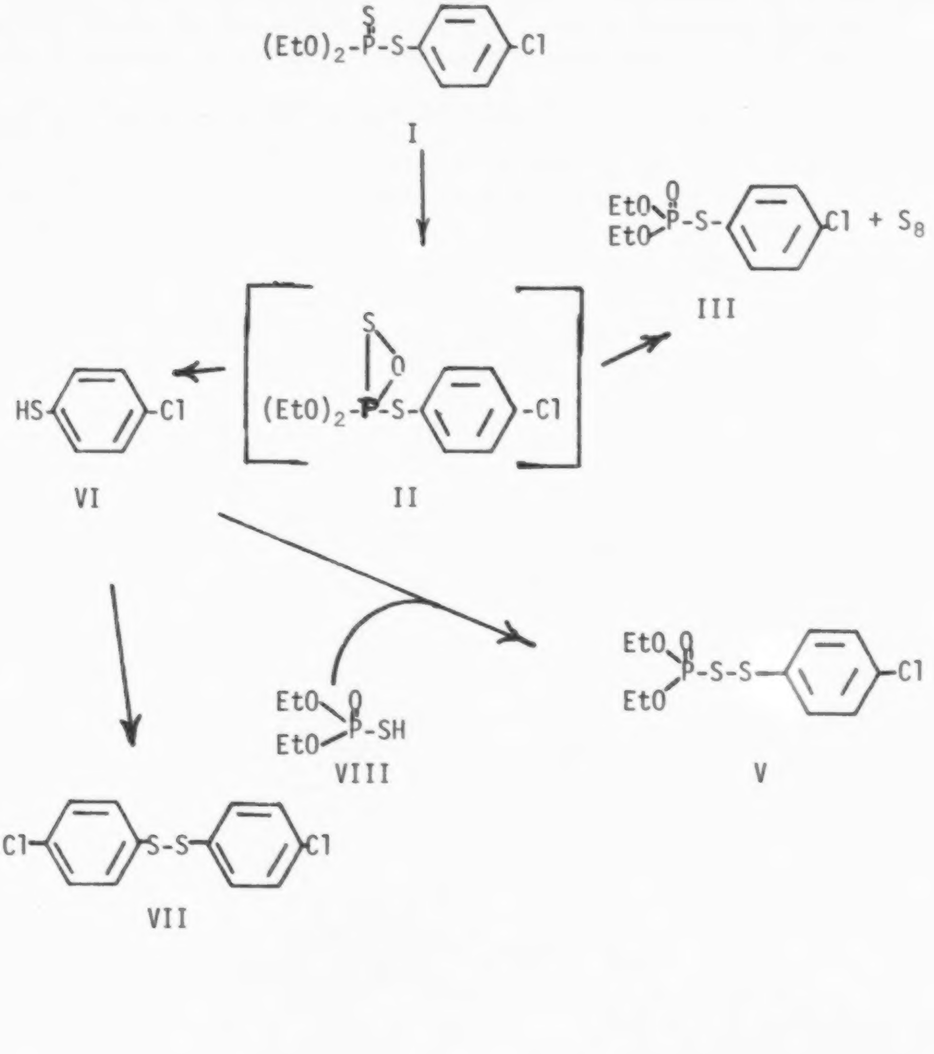


DIFENZOQUAT [1,2-Dimethyl-3,5-diphenyl-1-H-pyrazolium]

Difenzoquat was applied to foliage of wild oat (*Avena fatua* L.), barley (*Hordeum vulgare* L.), and wheat (*Triticum vulgare* L.). In the presence of surfactants, penetration was rapid and in excess of 80% within 72 h. Analyses up to 15 days after treatment, revealed no difenzoquat metabolism (Sharma et al., 1976).

O,*O*-Diethyl *S*-(4-chlorophenyl)phosphorodithioate

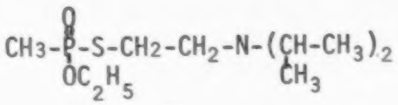
3-Chloroperbenzoic acid was used to oxidize this compound in an attempt to elucidate phosphinyl disulfide formation from a phosphorodithioate ester. Analyses indicated the formation mainly of the oxon (III), sulfur (IV) and disulfide (V), and compound VI, VII and VIII in smaller amounts. These studies also indicated that a "phosphorus oxythionate" (II) occurred as an unstable intermediate (Miyamoto and Yamamoto, 1977).


(EtO)2-P-S-Cl
I
EtO EtO P-S-Cl + S8
III
HS-Cl
VI
(EtO)2-P-S-Cl
II
EtO EtO P-SH
VIII
EtO EtO P-S-S-Cl
V
Cl-S-S-Cl
VII

S-2-(Diisopropylamino)ethyl O-ethyl methylphosphonothiolate

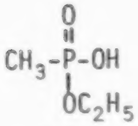
The degradation of this compound was studied in humic sand, humic loam, and clayey peat. The only P-containing products observed were methylphosphonic acid and ethyl methylphosphonate. The fate of the remainder of the molecule was not determined (Verweij and Boter, 1976).

The subject compound (I) hydrolyzed rapidly to ethyl hydrogen methylphosphonate (II) and methylphosphonic acid (III). In alkaline methanol extracts of humic sand, compound V was identified by GLC and confirmed by GC-MS. In ancillary studies with soil treated with compound IV, rapid oxidation of IV to V was observed (Kaaijk and Frijlink, 1977).



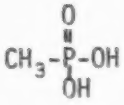
$CH_3\text{-}\overset{O}{\underset{OC_2H_5}{P}}\text{-}S\text{-}CH_2\text{-}CH_2\text{-}N\text{-}(\underset{CH_3}{CH}\text{-}CH_3)_2$

I



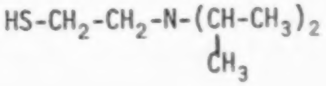
$CH_3\text{-}\overset{O}{\underset{OC_2H_5}{P}}\text{-}OH$

II



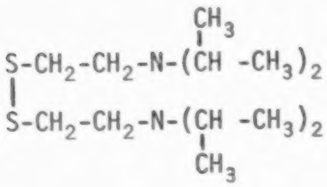
$CH_3\text{-}\overset{O}{\underset{OH}{P}}\text{-}OH$

III

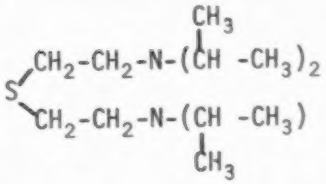


$HS\text{-}CH_2\text{-}CH_2\text{-}N\text{-}(\underset{CH_3}{CH}\text{-}CH_3)_2$

IV



V



VI

DIMETHOATE [O,O-Dimethyl S-(N-methylcarbamoylmethyl)phosphorodithioate]

After male Sprague-Dawley rats were exposed to dimethoate, analysis of collected urine indicated the presence of O,O-dimethyl phosphoric acid, O,O-dimethyl phosphorothioic acid, and O,O-dimethyl phosphorodithioic acid (Bradway et al., 1977).

Inducers of hepatic enzymes increased the amount of dimethoxon recovered in urine of treated mice (Tseng, 1973).

Analyses of cherries 28 to 35 days after treatment with dimethoate showed the presence only of dimethoate and its oxon metabolite (Zwick et al., 1977).

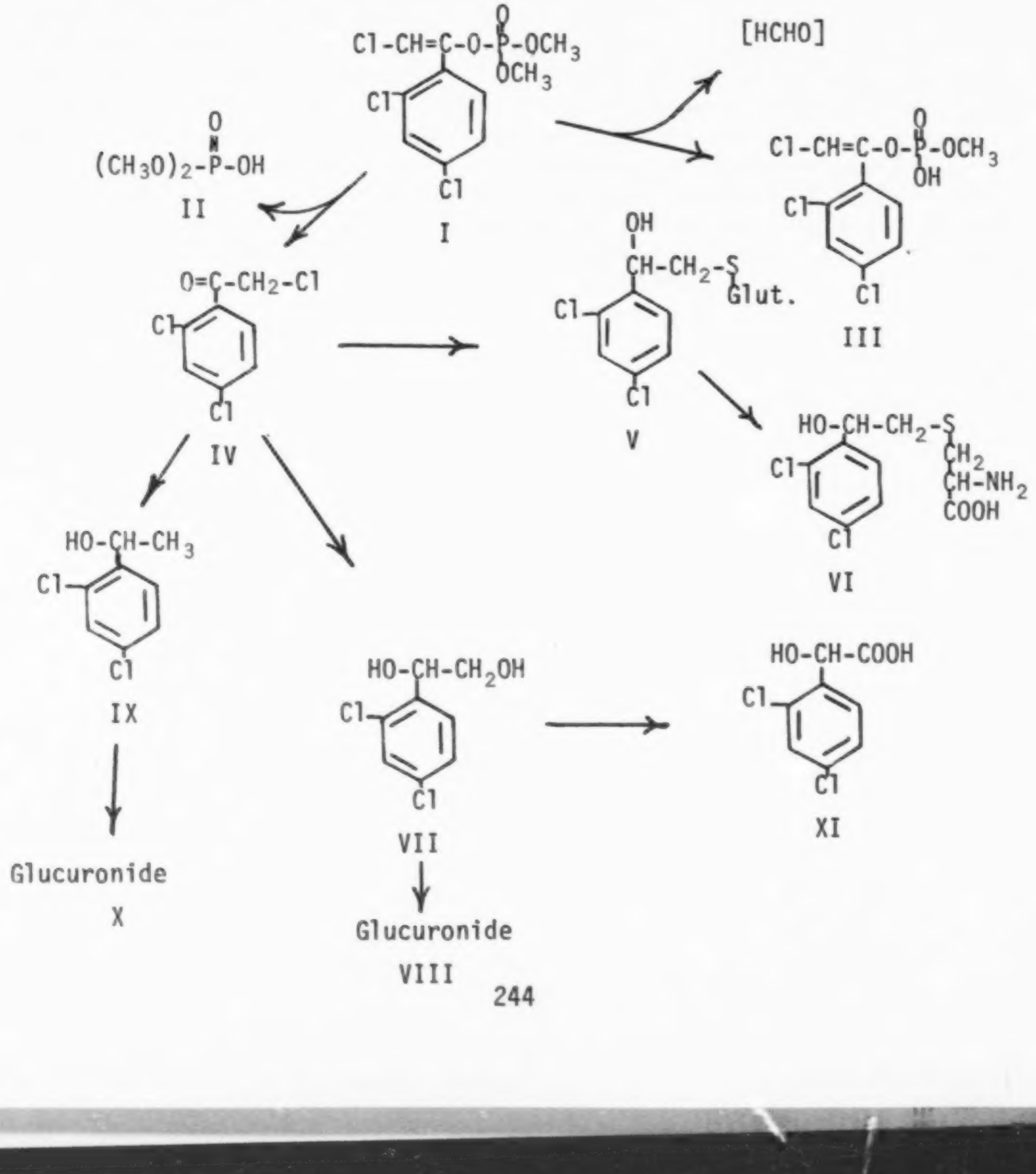
The loss of dimethoate applied to soil by evaporation and co-distillation was substantial. For a given application, it was also found that loss by leaching was in the order clay < clay loam < loam < sandy clay loam < sand (El Beit et al., 1977). Temperature and pH also were important in affecting stability of dimethoate in water and soil. In the pH range 7-11, dimethoate degradation depended on alkalinity (El Beit et al., 1978b). In alkaline clay soil, hydrolysis was followed by oxidation. Of nine metabolites extracted from soil, six were identified as desmethyl dimethoate, dimethoate carboxylic acid, dimethyl phosphorodithioate, dimethyl phosphate, dimethyl phosphorothioate, and phosphate. Three other metabolites were tentatively identified as the desmethylthiocarboxy analog and two isomers of the desmethyloxycarboxy analog (El Beit et al., 1978a).

N,*N*'-Dimethyl phosphorodiamidate

When this compound was administered to rats and cows, the *N*-methyl-*N*'-formyl and *N*-demethyl analogs were observed in rat urine and cows' milk and identified with TLC, GC, GC/MS, NMR, and IR (Swann et al., 1976).

DIMETHYLVINPHOS [Dimethyl 2-chloro-1-(2,4-dichlorophenyl)vinyl phosphate]

When male and female rats were administered [^{14}C]dimethylvinphos (I), excretion accounted for 60-84% of the dose via urine and 10-30% via feces. Analyses by paper chromatography and TLC indicated the presence of glucuronides of 2,4-dichlorophenylethanediol (VIII) and 1-(2,4-dichlorophenyl)ethanol (X) as well as 2,4-dichloromandelic acid (XI). TLC and autoradiography also showed the presence of 2,4-dichlorophenacyl chloride (IV), desmethyl dimethylvinphos (III) and a compound believed to be 2-(2,4-dichlorophenyl)-2-hydroxyethyl mercapturic acid (VI). The latter was not observed in dogs. A compound believed to be S-(2,4-dichlorophenacyl)glutathione (V) was formed and could then give rise to the mercapturic acid conjugate (Crawford et al., 1976).



Cl-CH=C-O-P-OCH3
O
OCH3
Cl
Cl
I
[HCHO]
(CH3O)2-P-OH
O
II
Cl-CH=C-O-P-OCH3
O
OH
Cl
Cl
III
O=C-CH2-Cl
Cl
Cl
IV
OH
CH-CH2-S
Glut.
Cl
Cl
V
HO-CH-CH2-S
CH2
CH-NH2
COOH
Cl
Cl
VI
HO-CH-CH3
Cl
Cl
IX
Glucuronide
X
HO-CH-CH2OH
Cl
Cl
VII
Glucuronide
VIII
HO-CH-COOH
Cl
Cl
XI

DINITROANILINE

AC 92553 [N-(1-Ethylpropyl-2,6-dinitro-3,4-xylidine]

BENEFIN [N-Butyl-2,6-dinitro-N-ethyl-α,α,α-trifluoro-p-toluidine]

BUTRALIN [4-(1,1-Dimethylethyl)-2,6-dinitro-N-(1-methylpropyl)-benzenamine]

CHLORNIDINE (AN-56477) [N,N-Bis(2-chloroethyl)-2,6-dinitro-p-toluidine]

DINITRAMINE [N^3,N^3-Diethyl-2,4-dinitro-6-trifluormethyl-m-phenylenediamine]

FLUCHLORALIN [N-(2-Chloroethyl)-2,6-dinitro-N-propyl-α,α,α-trifluoro-p-toluidine]

GS 38946 [2,6-Dinitro-N-ethyl-N-tetrahydrofurfuryl-4-trifluoromethylaniline]

ISOPROPALINE [2,6-Dinitro-N,N-dipropylcumidine]

NITRALIN [2,6-Dinitro-N,N-dipropyl-4-methylsulfonylaniline]

ORYZALIN [3,5-Dinitro-N^4,N^4,dipropylsulfanilamide]

PENOXALIN [3,4-Dimethyl-2,6-dinitro-N-(1-ethylpropyl)benzenamine]

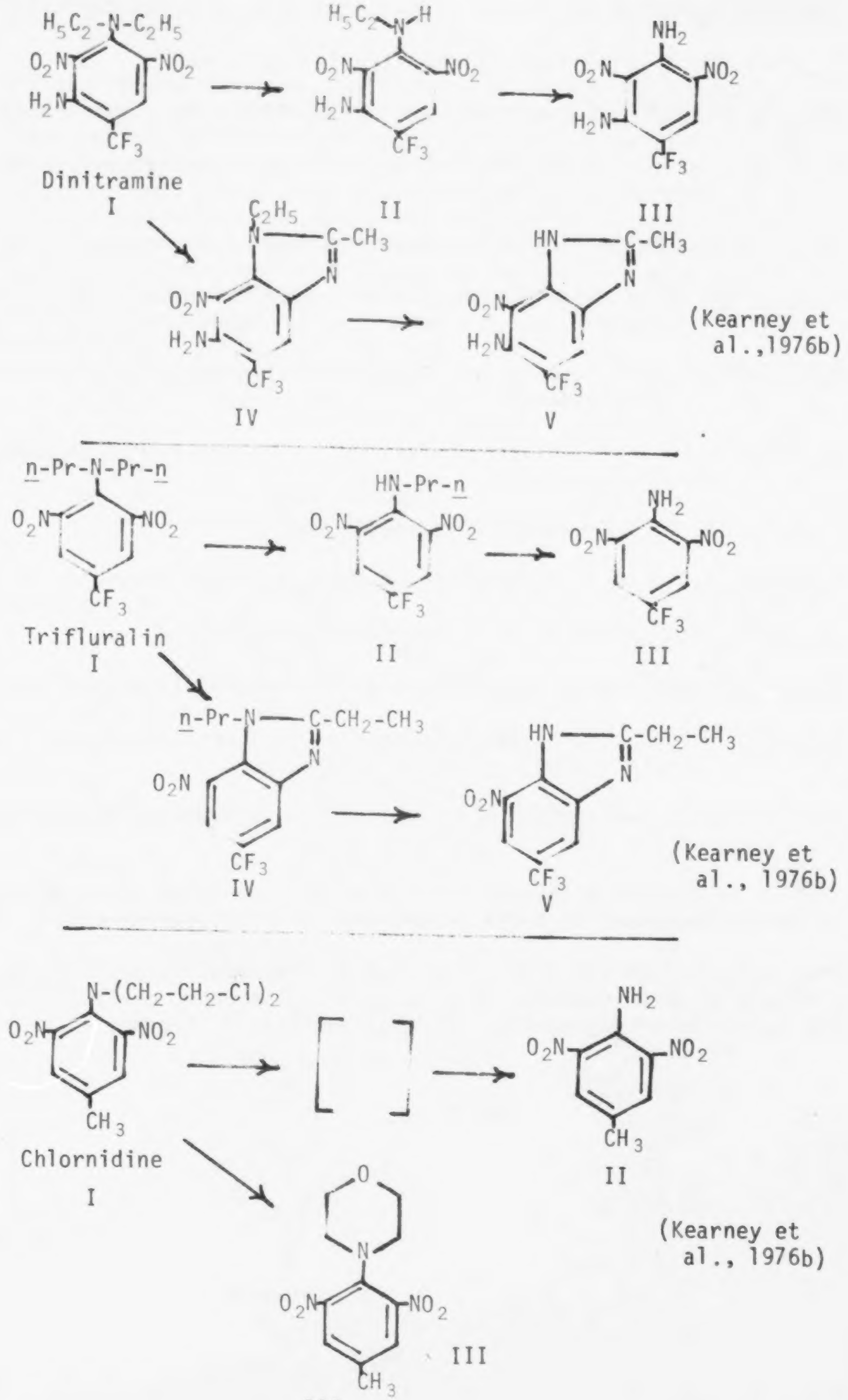
PROFLURALIN [N-Cyclopropylmethyl-2,6-dinitro-N-propyl-α,α,α-trifluoro-p-toluidine]

TRIFLURALIN [2,6-Dinitro-N,N-dipropyl-α,α,α-trifluoro-p-toluidine]

Studies in aquatic ecosystems indicated the formation of bound residues in Gambusia exposed to butralin and profluralin (Kearney et al., 1977a).

When butralin, chlornidine, dinitramine, fluchoralin, profluralin and trifluralin were incubated with Matapeake silt loam, analyses indicated the formation of degradation products see Fig. 1 (Kearney et al., 1976b).

Fig.1. Degradation in soils

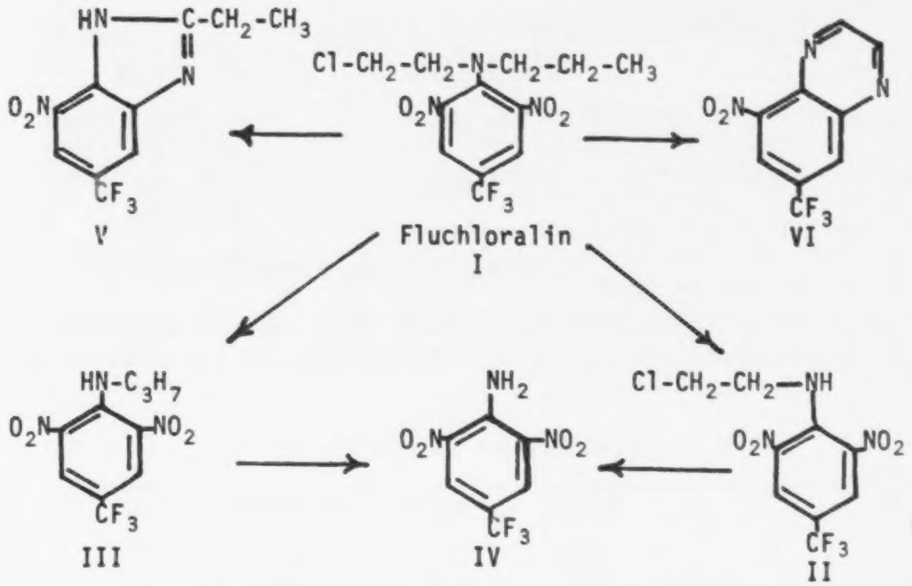

Dinitramine
I
II
III
IV
V
Trifluralin
I
II
III
IV
V
Chlornidine
I
II
III

(Kearney et al.,1976b)

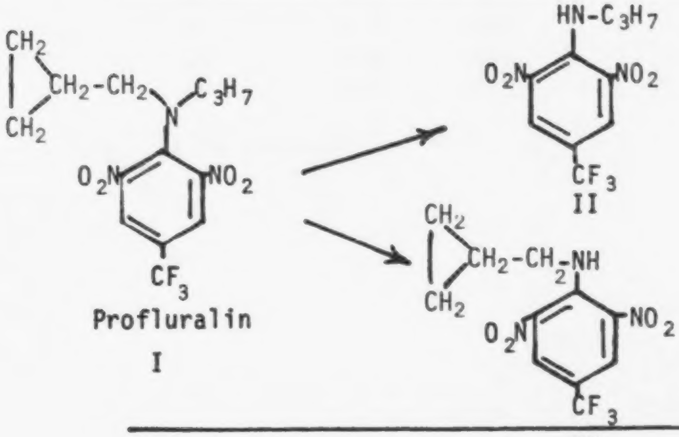
(Kearney et al., 1976b)

(Kearney et al., 1976b)

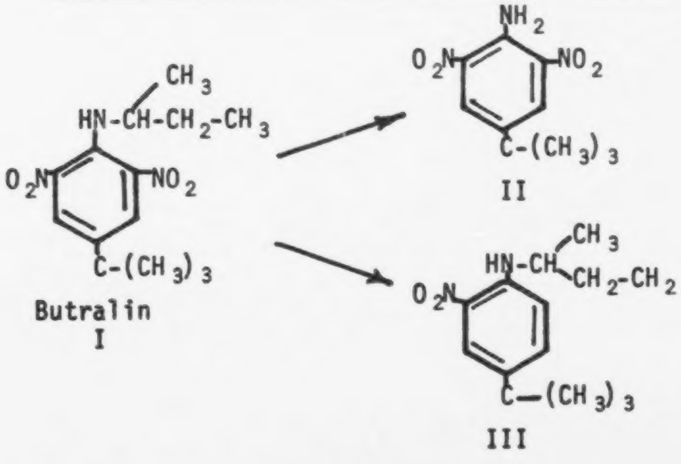
Fig. 1(cont.)


HN—C-CH2-CH3
N
O2N
CF3
V
Cl-CH2-CH2-N-CH2-CH2-CH3
O2N
NO2
CF3
Fluchloralin
I
O2N
N
N
CF3
VI
HN-C3H7
O2N
NO2
CF3
III
NH2
O2N
NO2
CF3
IV
Cl-CH2-CH2—NH
O2N
NO2
CF3
II

(Kearney et al., 1976b)


CH2
CH2-CH2
C3H7
CH2
N
O2N
NO2
CF3
Profluralin
I
HN-C3H7
O2N
NO2
CF3
II
CH2
CH2-CH2-NH
CH2
O2N
NO2
CF3
III

(Kearney et al., 1976b)


CH3
HN-CH-CH2-CH3
O2N
NO2
C-(CH3)3
Butralin
I
NH2
O2N
NO2
C-(CH3)3
II
CH3
HN-CH
CH2-CH2
O2N
C—(CH3)3
III

(Kearney et al., 1976b)

	$T_{1/2}$ Field Study	$T_{1/2}$ Lab. Study
Isopropalin	7-9 mos.	3.5 mos (30C) 13.3 mos (15C)
Oryzalin	1.5-2 mos.	1.4 mos (30C) 4.35 mos (15C)

(Gingerich and Zimdahl, 1976)

The distribution of dinitroaniline herbicides in an aquatic ecosystem was studied. Bioaccumulation ratios were determined and are summarized in Table 1.

Table 1. Bioaccumulation ratios

Herbicide	Algae	Snails	Daphnids	Fish
Butralin	236	304	77	74
Chlornidine	521	208	188	42
Dinitramine	329	279	74	83
Fluchloralin	291	324	95	32
Profluralin	218	609	88	39
Trifluralin	276	400	92	33

(Kearney et al., 1977a)

AC 92553 [N-(1-Ethylpropyl)-2,6-dinitro-3,4-xylidine]

Degradation of AC 92553 (I) in soils followed first-order kinetics. Calculated half-lives varied from 72 days to 172 days for seven soils examined. As the content of organic matter increased in the soils, there was a decreased rate of loss of herbicide. Similarly, decreased temperatures and/or soil moisture increased the half-life. In Sheep pens soil, the half-life at 30C was 98±3.2 days; at 10C, 409±27.9 days; at 25C and 75% soil moisture, 122±3.8 days; at 25C and 12.5% soil moisture, 563±88.2 days (Walker and Bond, 1977).

DINITRAMINE [N^3,N^3-Diethyl-2,4-dinitro-6-trifluoromethyl-*m*-phenylenediamine]

Carp (*Cyprinus carpio*) accumulated dinitramine when exposed to 1 mg/l of dinitramine. The presence of unchanged dinitramine was observed in plasma, muscle, and bile. The monoethyl and deethylated analogs were found in the gallbladder bile (Olson et al., 1977; Allen et al., 1978). The herbicide was not completely eliminated after 24 h in water free of dinitramine (Olson et al., 1975).

Plant metabolism of dinitramine was greater at 38C than at 16C in barnyard grass, gorghum and Palmer amaranth. This was not the case with soybean (Hawxby and Basler, 1976).

Dinitramine was applied to soil in which soybean plants were grown. A major soil metabolite was found at very low levels in the plants and identified as 6-amino-1-ethyl-2-methyl-7-nitro-5-trifluoromethylbenzimidazole (Belles and Smith, 1973).

FLUCHLORALIN (Basalin) [N-(2-Chloroethyl)-2,6-dinitro-N-propyl-α,α,α-trifluoro-p-toluidine]

Fluchloralin was extensively metabolized *in vitro* by normal and phenobarbital-induced rat liver microsomes. Metabolites produced indicated that fluchloralin metabolism involved N-dealkylation, aliphatic hydroxylation, nitro reduction and cyclization. Analyses with TLC and GC-MS indicated the formation of 2,6-dinitro-N-(n-propan-3-ol)-α,α,α-trifluoro-p-toluidine and the corresponding N-(n-propan-2-ol) analog. N-dealkylation of fluchloralin gave the des-2-chloroethyl analog and di- dealkylated analogs. Other metabolites observed included 2-amino-6-nitro-α,α,α-trifluoro-p-toluidine, 5-nitro-7-trifluoromethylquinoxaline, and 2-ethyl-7-nitro-5-trifluoromethyl benzimidazole (Nelson et al., 1976a and 1977a).

Soybean roots and shoots metabolized fluchloralin to at least 10 nonpolar metabolites, 6 polar metabolites, and some methanol-soluble residue. TLC, GLC, and MS were used to identify metabolites: 1-(2-chloroethyl)-2-ethyl-7-nitro-5-trifluoromethylbenzimidazole; α,α,α-trifluoro-N-(2-chloroethyl)-N-propyl-5-nitrotoluene-3,4-diamine, obtained from excised leaves and roots; 2-chloromethyl-7-nitro-1-propyl-5-trifluoromethylbenzimidazole; and 2-amino-N-(2-chloroethyl)-6-nitro-N-propyl-4-trifluoromethylaniline (Marquis, 1976 and 1977).

^{14}C-Fluchloralin was degraded in a loamy sand soil. Degradation products were identified by TLC and GLC and comparison with standard compounds whose structure was confirmed by IR and MS. Degradation products included the following compounds:

N-(2-Chloroethyl)-2,6-dinitro-4-trifluoromethylaniline
2,6-Dinitro-4-trifluoromethylphenol
2,6-Dinitro-4-trifluoromethylaniline
1,2-Diamino-6-nitro-4-trifluoromethylbenzene
1,2,3-Triamino-5-trifluoromethylbenzene
2,6-Dinitro-N-(2-hydroxypropyl)-N-propyl-4-trifluoromethylaniline
2,6-Dinitro-N-propyl-4-trifluoromethylaniline

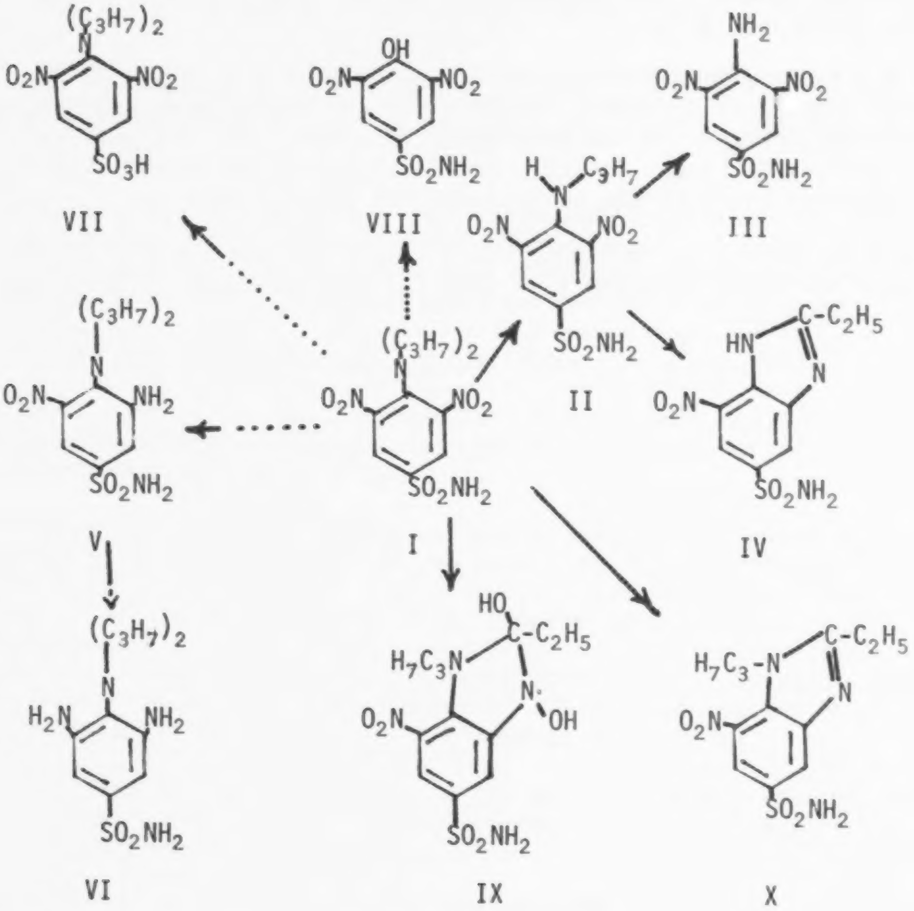
Some CO_2 was formed and a part of the ^{14}C was found in humic acids (Otto, 1974).

NITRALIN [2,6-Dinitro-N,N-dipropyl-4-methylsulfonylaniline]

Nitralin dissipated rapidly to low residual levels after application to soil. No accumulation was noted regardless of frequency (single or dual annual) or rate of application (Savage, 1973).

ORYZALIN [3,5-Dinitro-*N*^{4},*N*^{4}-di-*n*-propylsulfanilamide]

Soybeans and wheat were grown in soil treated with ^{14}C-oryzalin. Small amounts of ^{14}C were found associated with plant tissues but no products were identified. Analyses of the soil indicated rapid degradation of the ^{14}C-oryzalin. The most abundant compounds were metabolites II, X, and IV. Other products identified included compounds III, V, VI, VII, VIII and IX. The presence of polar compounds in the soil was also observed but none were identified (Golab et al., 1975).



PROFLURALIN (CGA-10832) [*N*-Cyclopropylmethyl-2,6-dinitro-*N*-propyl-α,α,α-trifluoro-*p*-toluidine]

Profluralin was extensively metabolized *in vitro* by normal and phenobarbital-induced rat liver microsomes. Metabolites produced indicated that profluralin metabolism involved *N*-dealkylation, aliphatic hydroxylation, nitro reduction and cyclization. Analyses with TLC and GC-MS indicated the formation of 2,6-dinitro-*N*-(*n*-propan-3-ol)-α,α,α-trifluoro-*p*-toluidine and the corresponding *N*-(*n*-propan-2-ol) analog. *N*-dealkylation of profluralin gave the des-*n*-propyl and di-dealkylated analogs and 2-ethyl-7-nitro-5-trifluoromethyl benzimidazole (Nelson et al., 1976a and 1977a).

Soil was treated with profluralin at the rate of 1.5 lb a.i./A and used to grow rotation crops. Profluralin and dealkylated and reduced analogs were present in the soil after 78 weeks. All metabolites contained the CF group intact. Profluralin and its metabolites were strongly bound to the soil (Honeycutt et al., 1978).

Hydrolysis studies at 20C indicated a $t_{1/2}$ = 29 days for 0.1 N NaOH; 150 days for 0.1 N HCl; and 1200 days for deionized water (Marco and Dupre, 1973).

TRIFLURALIN (Treflan, TFN) [2,6-Dinitro-*N*,*N*-dipropyl-α,α,α-trifluoro-*p*-toluidine]

Trifluralin was extensively metabolized *in vitro* by normal and phenobarbital-induced rat liver microsomes. Analyses with TLC and GC-MS indicated the formation of 2,6-dinitro-*N*-(*n*-propan-3-ol)-α,α,α-trifluoro-*p*-toluidine and the corresponding *N*-(*n*-propan-2-ol) analog. *N*-dealkylation of trifluralin gave the mono- and di- dealkylated analogs. Other metabolites observed included the *N*-propyl *N*-(*n*-propan-3-ol) and *N*-propyl *N*-(*n*-propan-2-ol) analogs, 2-amino-6-nitro-α,α,α-trifluoro-*p*-toluidine and 2-ethyl-7-nitro-5-trifluoromethyl benzimidazole (Nelson et al., 1976a and 1977a).

The dealkylated metabolite of trifluralin was metabolized by a mixture of two soil *Streptomyces* sp. Metabolites observed and tentatively identified included a diamine, an azobenzene, and azoxybenzene (Lusby et al., 1978).

A bacterium was isolated that decomposed trifluralin in the presence of glutamate, lactate, acetate and yeast extract. Optimal pH was 6.5 for bacterial growth and maximum trifluralin decomposition occurred at pH 7.4. Breakdown was accelerated in the presence of H-donors. Nitrite formation from nitro-groups appeared to be the first step in trifluralin degradation (Hamdi et al., 1969).

In soil, trifluralin was degraded to 3,4,5-triamino-α,α,α-trifluorotoluene which appeared to be a key metabolite in formation of soil bound residues (Golab et al., 1978).

Trifluralin dissipated rapidly to low residual levels after application to soil. No accumulation was noted regardless of frequency (single or dual annual) or rate of application (Burnside, 1974; Savage, 1973). Other studies with Congaree soil indicated strong adsorption to soil and a two step disappearance of trifluralin. Initially, the disappearance was rapid with a $t_{1/2} \approx 19$ days. Determination of the second stage indicated 99% residue loss in about 72 months with $t_{1/2} = 450$ days (LaFleur et al., 1978).

When applied to Egam and Beason soils, trifluralin degradation followed first-order kinetics with $t_{1/2} = 35.8$ and 25.7 days, respectively (Duseja and Holmes, 1978).

When trifluralin was released to the atmosphere, air sample analyses indicated rapid photochemical conversion to the dealkylated compound 2,6-dinitro-*N*-propyl-α,α,α-trifluoro-*p*-toluidine. The $t_{1/2}$ was calculated to be 20 minutes under midday summer sunlight. In fall, the $t_{1/2}$ lengthened to 193 minutes (Woodrow et al., 1978).

In a vapor-phase photoreactor, trifluralin was transformed by successive N-dealkylation to 2,6-dinitro-4-trifluoromethylaniline and by an internal condensation to 2-ethyl-7-nitro-1-propyl-5-trifluoromethylbenzimidazole. This also underwent an N-dealkylation (Moilanen and Crosby, 1974). These four compounds were detected in air above a field which had been treated with trifluralin (Crosby et al., 1974).

DINITRO COMPOUNDS

DINOSEB [2-*sec*-Butyl-4,6-dinitrophenol]

DNOC [2-Methyl-4,6-dinitrophenol]

Dinoseb and DNOC were incubated with *Azotobacter* sp. Dinoseb was converted to 6-acetamido-2-*sec*-butyl-4-nitrophenol. DNOC was converted to the corresponding 6-acetamido analog. The 6-aminophenols of both compounds were observed only at the beginning and were almost immediately acetylated (Wallnofer et al., 1978).

In pure cultures, *Pseudomonas* sp. and *Arthrobacter* sp. converted DNOC to 2,3,5-trihydroxytoluene prior to ring cleavage. With *Pseudomonas* sp., 3-methyl-5-nitrocatechol formed and was reduced to 3-methyl-5-amino-catechol. *Corynebacterium simplex* degraded DNOC to colorless matter and nitrite (Nehez et al., 1977).

DIOXATHION (Delnav, Hercules AC-528) [2,3-p-Dioxanedithiol S,S-bis(O,O-diethyl phosphorodithioate)]

DIOXENETHION [2-p-Dioxenethiol S-(O,O-diethyl phosphorodithioate]

When applied to a Hereford steer, delnav was degraded and analysis of urine indicated the presence of diethyl phosphoric acid, diethyl phosphorothioic acid, and diethyl phosphorodithioic acid. With the exception of hair, hide and liver, tissue residues 7 days after application were less than 0.5 ppm. Administration of cis- and trans-P^{32}-delnav to mice gave the same hydrolytic products (Plapp et al., 1960).

Both trans- and cis-dioxathion and dioxenethion underwent little or no metabolism by rat liver microsomal preparations unless fortified by NADPH. TLC cochromatography of ether extracts of incubation mixtures indicated the presence of the following metabolites:

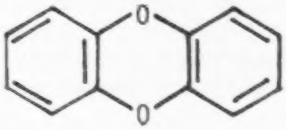
I. t- and c- dioxadioxon
II. t- and c- dioxaoxon
III. dioxenoxon
IV. O,O-diethyl phosphorodithioic acid (ESSP)
V. O,O-diethyl phosphorothiolate (ESOP)
VI. O,O-diethyl phosphoric acid (EOOP)

A number of other metabolites were observed but not identified (Harned and Casida, 1976).

When labeled dioxathion was orally administered to rats, most of the label was excreted within 96 h. Compounds IV, V and VI were observed (Harned and Casida, 1976).

On glass surfaces, volatilization half-lives were dioxenethion, <30 min; and dioxathion, ca 32 days. After application of t-dioxathion, residues consisted of unreacted material, dioxaoxon, dioxadioxon, EOOP and unidentified material. On silica gel and exposure to sunlight, residues consisted of dioxaoxon, dioxadioxon, ESSP, ESOP, EOOP, ethylene glycol, and unidentified material. When dioxenthion was applied to bean leaves, 60-70% of the ^{14}C disappeared within one day. Residues consisted of dioxenthion, dioxeneoxon, and EOOP. Dioxathion was more persistent. In addition to some EOOP, residues consisted of dioxaoxon and dioxadioxon (Harned and Casida, 1976).

DIOXIN [Dibenzo-p-dioxin]



After a single oral dose administration of ^{14}C-TCDD to rats, ^{14}C was detected in feces but not urine with a body $t_{1/2}$=31 6 days (Rose et al., 1976).

Rats were treated with phenobarbital and then hepatic microsomal preparations were made. When TCDD was incubated with these, binding of TCDD to solids of the microsomal incubation mixture was observed (Nelson et al., 1977b).

Dioxins were administered to rats. Urine and feces were collected and analyzed. Dibenzo-p-dioxin yielded the 2-hydroxy analog, one methylthio and one dihydroxy analog. 1-Chlorodibenzo-p-dioxin yielded 4-monohydroxy analog, one methylthio and two dihydroxy metabolites. 2-Chlorodibenzo-p-dioxin yielded the 3-monohydroxy analog, one methylthio and two dihydroxy metabolites. 2,3-Dichlorodibenzo-p-dioxin yielded the 7-hydroxy analog and two dihydroxy metabolites. 2,7-Dichlorodibenzo-p-dioxin yielded two monohydroxy, one monochloro-dihydroxy and one dihydroxy metabolite. 1,2,4-Trichlorodibenzo-p-dioxin yielded one monohydroxy and one dihydroxy metabolite. 1,2,3,4-Tetrachlorodibenzo-p-dioxin yielded the 7-hydroxy analog and two dihydroxy metabolites. Octachlorodibenzo-p-dioxin was not metabolized. Because the analytical procedures involved hydrolysis and methylation, the methylthio metabolites could have formed from glutathione or mercapturic acid derivatives during the work-up (Tulp and Hutzinger, 1978).

When labeled 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) was studied in a model aquatic environment, the total percent recovery of ^{14}C-TCDD decreased with time and a half-life of TCDD in the sediment was calculated to be 600 days. When added to lake water alone, the data indicated that about 71% of the radioactivity was recovered after 589 days. Metabolism of TCDD was very low, not more than 4%, and apparently involved microbial activity (Ward and Matsumura, 1978).

When TCDD was exposed to natural sunlight on leaves, soil or glass plates, photodechlorination was responsible for loss of most of the TCDD and produced traces of dichloro- and trichlorobenzo-p-dioxins

(Crosby and Wong, 1976). When adsorbed on Kieselgel and exposed to UV, 98% of the TCDD was destroyed after 4 days when a quartz filter was used; 92% after 7 days when a pyrex filter was used (Gebefugi et al., 1977). Exposure of TCDD to summer sunlight on silica produced a polar product in about 37% yield. On soil similarly exposed, the yield was about 6% with no difference between exposed and unexposed TCDD. Soil seemed to limit photolysis (Plimmer, 1978). TCDD photodegradation occurred in the presence of a system that acted as a hydrogen donor, such as waxy cuticles of green leaves as well as oily or aromatic solvents. A suitable system was obtained by spraying surfaces with 1:1 xylene-ethyl oleate solution (Liberti et al., 1978). 1-Hexadecylpyridinium chloride, a cationic surfactant, also acted as an energy transfer agent and increased the TCDD photodecomposition rate (Botre et al., 1978).

Irradiation of TCDD in an organic solvent by γ-rays produced tri- and di- chlorodibenzo-*p*-dioxins (Fanelli et al., 1978).

When wood chips with high water content were present, the temperature of the flue gas duct dropped and combustion of a 2,4,5-T formulation produced small amounts of polychlorinated dibenzo-*p*-dioxins and dibenzofurans (Ahling et al., 1977).

A chlorophenol formulation containing 2,4,6-tri-, 2,3,4,6-tetra-, and pentachlorophenate was sprayed on birch leaves and wood wool and burned after overnight drying. Results were qualitatively similar, yielding tetra-, penta-, hexa-, hepta-, and octa- chlorodibenzo-*p*-dioxins. Burning each of the purified chlorophenates gave the same products. Identification of the dioxins formed is summarized.

Chlorinated dibenzo-*p*-dioxins

1,3,6,7-Cl_4
1,3,7,9-Cl_4
2,3,7,8-Cl_4
1,2,3,8 or 1,2,3,7-Cl_4
1,2,6,9-Cl_4
1,2,6,7-Cl_4
1,2,8,9-Cl_4
1,2,4,7,8-Cl_5
1,2,3,4,7-Cl_5
1,2,3,7,8-Cl_5

1,2,4,6,7,9-Cl_6 or 1,2,4,6,8,9-Cl_6
1,2,3,4,6,8-Cl_6
1,2,3,6,8,9-Cl_6 or 1,2,3,6,7,9-Cl_6
1,2,3,4,6,9-Cl_6
1,2,3,4,7,8-Cl_6
1,2,3,6,7,8-Cl_6
1,2,3,7,8,9-Cl_6
1,2,3,4,6,7-Cl_6
1,2,3,4,6,7,9-Cl_7
1,2,3,4,6,7,8-Cl_7
Cl_8

Three pentachlorodibenzo-*p*-dioxins from pyrolysis of 2,4,6-tri- and 2,3,4,6-tetrachlorophenate were not further characterized (Rappe et al., 1978).

DIPHENAMID (DPA) [*N*,*N*-Dimethyl-2,2-diphenylacetamide]

Aquatic plants and algae were exposed to diphenamid in trays and jars. The vascular plants and aquatic algae absorbed and removed diphenamid from the water. In algae, water hyacinth, and parrotfeather, *N*-methyl-2,2-diphenylamide (MDA) and other unidentified materials were observed (Bingham and Shaver, 1977).

Pepper plants (*Capsicum frutescens* L.) were treated with diphenamid or several analogs. The major metabolites of diphenamid were isolated and identified with chromatography and mass spectra as compounds II-XII. Simultaneous exposure to ozone did not affect diphenamid absorption or translocation significantly. Accumulation of compounds more polar than metabolite XI was observed in leaves but reduced the accumulation of these in roots (Hodgson and Hoffer, 1977a and b).

When tomato plants treated with DPA were fumigated with ozone, a metabolite formed and was identified as the *O*-gentiobioside. In addition to this, the *N*-methyl analog and the *N*-hydroxymethyl-*N*-methyl metabolite were also observed (Hodgson *et* al., 1973).

In cotton, okra, peanut shoots, and soybean shoots, dealkylated products and water-soluble compounds were present. Brightleaf and burley tobacco shoots also had dealkylated products. In cotton, okra, peanut and soybean shoots, the presence of the glucoside (MDAG) and gentiobioside (MDAGB) were observed (Hodgson and Hoffer, 1976).

The metabolism of diphenamid in cell suspensions of soybeans was studied. When ^{14}C-carbonyl-labeled diphenamid was added to the suspensions, the major products were identified as *N*-hydroxymethyl *N*-methyl-2,2-diphenylacetamide, *N*-methyl-2,2-diphenylacetamide, 2,2-diphenylacetamide, an unidentified glucoside, and an acidic conjugate of glucose, malonate and diphenamid (Davis et al., 1978).

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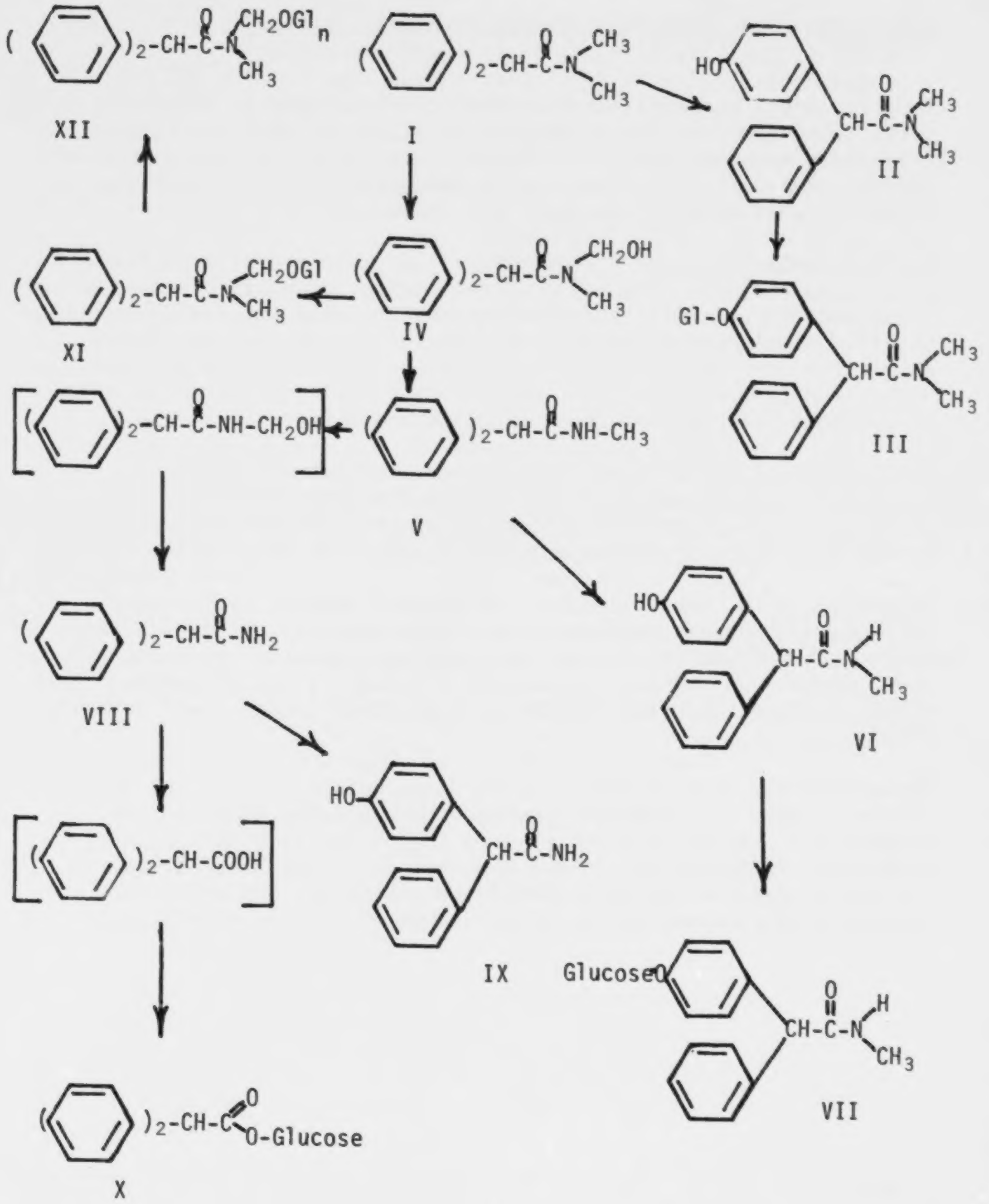

XII
I
II
XI
IV
III
V
VI
VIII
IX
VII
X
CH2OGl n
Gl-O
Glucose O
O-Glucose

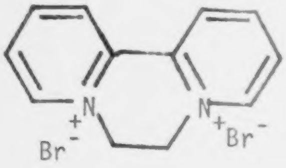
DIQUAT [1,1'-Ethylene-2,2'-bipyridylium dibromide]

PARAQUAT (Gramoxone) [1,1'-Dimethyl-4,4'-bipyridylium dichloride]

When incubated with rat tissues, paraquat binding to acid precipitable protein occurred. Binding was greater with lung protein than with liver, heart, kidney or spleen (Hollinger and Giri, 1978).

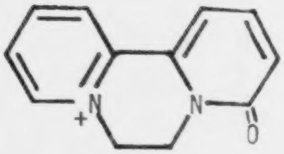
Applied paraquat resided in the top one cm of sandy loam soil. When incubated at 25C for up to 16 months, there was no evidence of chemical or microbiological degradation (Smith and Mayfield, 1978).

^{14}C-Diquat, fed to hens, was excreted mainly (70-80%) as unchanged diquat in feces. Two metabolites were identified in feces as 9-oxo-6,7-dihydro-8H-dipyrido[1,2-a:2',1'-C]-5-pyrazinium ion (II), and 1-oxo-1,2,3,4-tetrahydro-2H-pyrido[1,2-a]pyrazinium ion (III) in 4% and 2% amounts, respectively. These metabolites were also present in eggs in trace amounts (0.015 ppm and 0.0008 ppm, respectively) when hens were fed 4-5 ppm in the diet (Leahey and Hemingway, 1974).

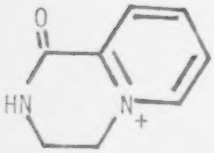


Diquat

I



II



III

DISULFIRAM (DSF, TTD, Tetraethylthiuram disulfide) [Bis(N,N-diethylthiocarbamoyl)disulfide]

When disulfiram was administered orally to rats, diethyldithiocarbamate appeared in the intestines (Blanquat et al., 1976). In humans, metabolism of disulfiram produced diethylamine. The latter appeared in urine (Neiderhiser et al., 1976).

When administered i.p. to mice, S^{35}-disulfiram (DSF) was rapidly metabolized to diethyldithiocarbamate (DDC) and its methyl ester (DDC-Me), DDC-glucuronide and inorganic sulfate. DDC was observed in plasma, lung, liver, kidney and brain; DDC-Me, in liver, kidney, plasma, brain and lung. The glucuronide and sulfate were observed in plasma, brain, lung, liver and kidney as soon as 5 minutes after administration (Faiman et al., 1978).

After i.p. administration of S^{35}-DSF to a dog, S^{35}-DDC-glucuronide and inorganic sulfate were observed in urine. DDC and DDC-Me were observed in plasma as were DDC-glucuronide and inorganic sulfate (Faiman et al., 1978). About 25% of an intravenous administration of DDC to a dog was S-methylated. This exhibited a first-order rate with a calculated $t_{1/2}$ = 12.2 minutes (Cobby et al., 1978).

DITHIOCARBAMATES

ETU [Ethylenethiourea]

FERBAM [Ferric dimethyldithiocarbamate]

MANEB [Manganese ethylenebisdithiocarbamate]

METHAM-SODIUM [Sodium *N*-methyldithiocarbamate]

NABAM [Disodium ethylenebisdithiocarbamate]

PROPINEB [Zinc *N*,*N*'-propylene-1,2-bis(dithiocarbamate)]

ZINEB [Zinc ethylenebisdithiocarbamate]

ZIRAM [Zinc dimethyldithiocarbamate]

Additional evidence for the structure of ethylenethiuram monosulfide, as shown, was derived from chemical, IR and NMR studies (Alvarez et al., 1973).

After application of ethylenebis(dithiocarbamates) (EBDC) on tomatoes, ETU was detected on the tomatoes (Ripley and Cox, 1978).

DITHIOCARBAMATE

FERBAM (Fermate) [Ferric dimethyldithiocarbamate]

^{35}S- and ^{3}H-labeled ferbam were administered to sheep. The ^{35}S was not eliminated as CS_2. 76 h post treatment, about 12% of the ^{35}S and 62% of ^{3}H had been excreted. Although a number of metabolites, polar and non-polar, were observed, none were identified. Neither TMTD nor dimethylamine were present (Hunt and Gilbert, 1976).

^{35}S- and ^{14}C-labeled ferbams were administered as an oral dose to rats. After absorption through the gastrointestinal tract, ^{35}S activity was observed in urine (22.7%), expired air (18.1%), bile (1.0%), and small amounts in tissues. When [^{14}C]ferbam was used, ^{14}C was found in urine (42.9%, bile (1.4%), expired air (0.6%), and small amounts in tissues. The metabolite in expired air was identified as carbon disulfide. In the urine, inorganic sulfate, a dimethylamine salt, and a dimethyldithiocarbamate glucuronide were identified (Hodgson et al., 1975).

DITHIOCARBAMATES

MANEB [Manganese ethylenebisdithiocarbamate]

Maneb residues on tomato and bean plants decreased rapidly after application. The half-life of maneb in soil was found to be 4 to 8 weeks (Rhodes, 1977a).

In some field studies, after application of maneb to a variety of crops, no residues of ETU were observed (Pease and Holt, 1977). In field studies, after application of maneb to tomatoes, ETU, ethylenethiuram monosulfide, and ethylenebis(isothiocyanate) residues were observed (Newsome, 1976).

Studies with maneb, after application to soybeans, indicated the formation of ethyleneurea, 2,4-imidazolidinedione, 1-(2-imidazolin-2-yl)-2-imidazolidinethione,, and several other unidentified compounds (Nash, 1976).

Vegetables were fortified with maneb, and then cooked. In all cases, significant amounts of ETU formed (Watts et al., 1974).

DITHIOCARBAMATES

METHAM-SODIUM (Vapam) [Sodium N-methyldithiocarbamate]

The conversion rate of metham-sodium to methyl isothiocyanate in soil was dependent on soil type and temperature and the half-life varied up to several weeks. In soil the conversion was apparently complete after only a few hours (Smelt and Leistra, 1974).

Degradation of vapam and methylisothiocyanate (MIT) in soils followed first-order kinetics. Breakdown of vapam and MIT followed first-order kinetics; and the breakdown of vapam to MIT was generally less than 30 minutes (Gerstl et al., 1977).

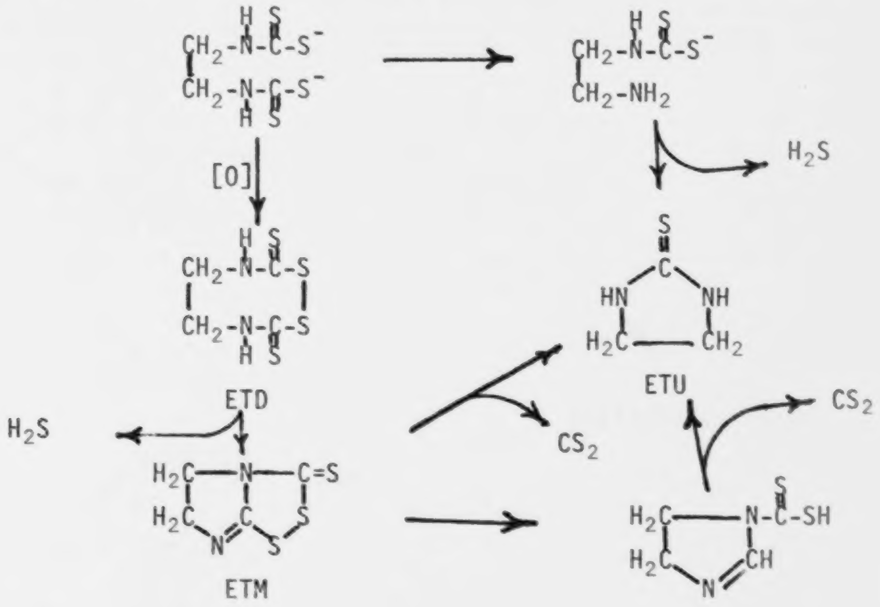
DITHIOCARBAMATES

NABAM [Disodium ethylenebisdithiocarbamate]

In an investigation of the kinetics of thermal decomposition of nabam in aqueous media, it was found that the rate of conversion of nabam to ETU was dependent upon temperature, O_2, and pH. A degradation scheme was proposed. ETM and β-aminoethyldithiocarbamate were confirmed as intermediates. Ethylene diisothiocyanate was not observed (Marshall, 1977b).

Studies with nabam, after application to soybeans, indicated the formation of ethyleneurea, 2,4-imidazolidinedione, 1-(2-imidazolin-2-yl)-2-imidazolidinethione, and several other unidentified compounds (Nash, 1976).

In an aqueous solution, nabam decomposed to form DIDT and ETU. Only ETU entered the plant. Within 19 days, however, ETU in the solution was converted to 2-imidazoline and ethyleneurea. When labeled nabam was applied to cucumber leaves, after 2 weeks about 65% of the activity was mainly in the form of ETU, DIDT and unidentified polar material. Ethyleneurea (EU) and 2-imidazoline were present in small amounts (Sijpestijn and Vonk, 1974).

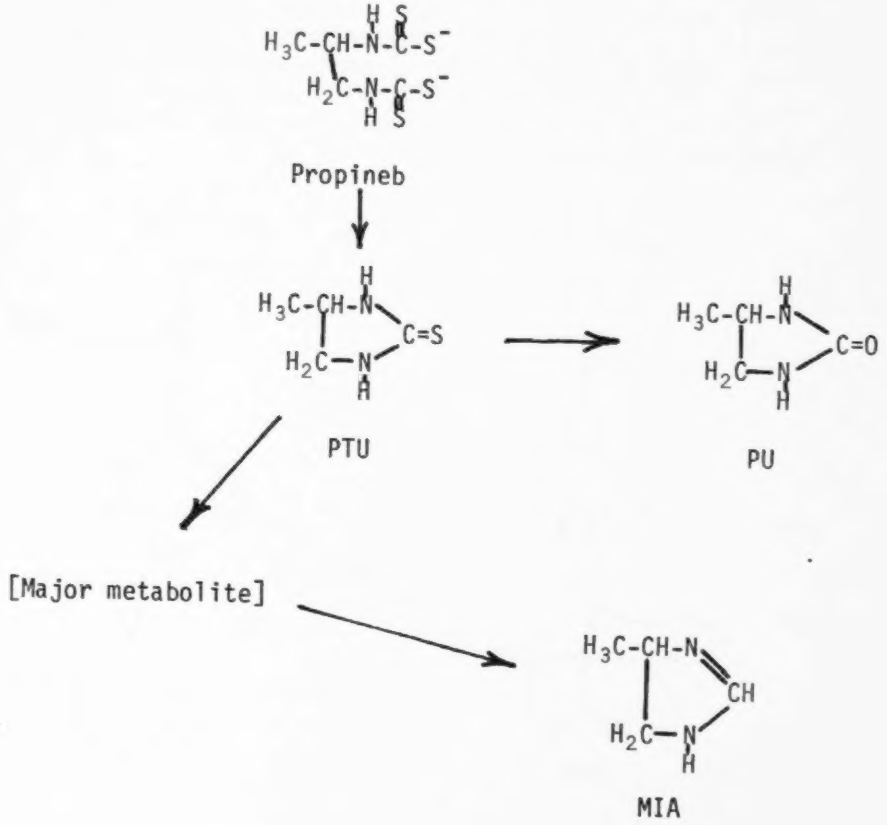


DITHIOCARBAMATES

PROPINEB (Antracol) [Zinc *N*,*N*'-propylene-1,2-bis(dithiocarbamate)]

Apples and grapes were treated with propineb. A major metabolite was not identified. Other metabolites observed were propylene urea (PU), propylene thiourea (PTU), and a compound believed to be 4-methylimidazoline (MIA). When PTU and ethylene thiourea (ETU) were applied, degradation proceeded rapidly. Metabolites of ETU were ethylenediamine (EDA), imidazoline, and EU (Voegler et al., 1977).

The fate of propineb in soil was studied. After spray application to soil, loss was mainly the result of mineralization (Mittelstaedt and Fuhr, 1977).



DITHIOCARBAMATES

ZINEB [Zinc ethylenebisdithiocarbamate)

After application of zineb to Concord grapes, residues of ETU were observed (Ripley et al., 1978). Similarly, after application to Bartlett pears, zineb gave rise to ETU residues. Dissipation of zineb was faster in the first day after application than in subsequent days (Ripley and Simpson, 1977).

Studies with zineb, after application to soybeans, indicated the formation of ethyleneurea, 2,4-imidazolidinedione, 1-(2-imidazolin-2-yl)-2-imidazolidinethione, and several other unidentified compounds (Nash, 1976).

In field studies, after application of zineb 75W to tomatoes, ETU, ethylenethiuram monosulfide, and ethylenebis(isothiocyanate) residues were observed (Newsome, 1976). When zineb was applied to lettuce, TLC showed the presence of ETU, EU, 2-imidazoline, 5,6-dihydroimidazo [2,1-C]dithiazole-3-thione (DIDT), ethylenediamine, and imidazolidine-2,4-dione. Boiling of some zineb metabolites produced ETU (Vonk, 1978).

In basic medium, oxidation of zineb with hypochlorite produced sulfate, CO_2 and EU. Oxidation of ethylenethiuram monosulfide (ETM) produced sulfate and EU (Marshall, 1978).

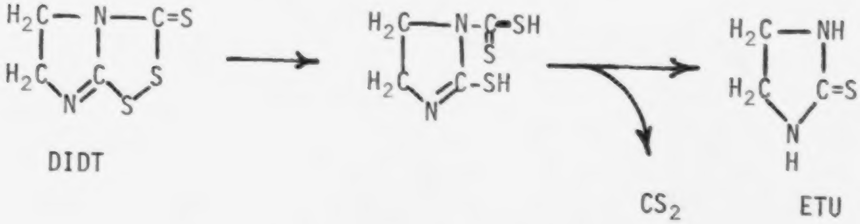
DITHIOCARBAMATES

ETU [Ethylenethiourea]

After treatment of tomato and bean plants with ETU, residues of ETU rapidly decreased. The degradation products of ETU on tomato plants were identified as ethyleneurea and 1-(2-imidazolin-2-yl)-2-imidazolidinethione. There also was an indication that imidazoline was present. When [^{14}C]ETU was applied to soil, analyses indicated that the half-life of ETU and its degradation products was less than 4 weeks under field conditions. Exposure of aqueous ETU solutions to mercury vapor UV light rapidly converted ETU to other compounds. Products observed were identified as ethyleneurea, hydantoin, glycine sulfate, and 1-(2-imidazolin-2-yl)-imidazolidinethione (Rhodes, 1977).

After administration of ETU to rats, elimination was mainly via urine, about 82.5% in 2 days. Fecal elimination accounted for only about 0.5% in 2 days. $^{14}CO_2$ was observed when 4,5-^{14}C-ETU was administered. When 2-^{14}C-ETU was used, only a tract of $^{14}CO_2$ was found. Eight metabolites of ETU were observed but not identified (Kato et al., 1976). In other studies, the $t_{1/2}$ of ETU elimination in rats was 9.4 h; in mice, 5.5 h. Metabolites were observed but not identified (Ruddick et al., 1977).

DIDT (5,6-dihydro-3-H-imidazo[2,1-C]-1,2,4-dithiazole-3-thione) forms spontaneously from ethylenebisdithiocarbamates. Washed suspensions of *P. fluorescens* were incubated with DIDT. ETU formation was observed by TLC. Washed suspensions of *E. coli* and bakers yeast (*Saccharomyces cerevisiae*) and mycellium of *Aspergillus niger* also converted DIDT to ETU. Cell free extracts of *P. fluorescens* were prepared. Diallysis of these preparations reduced their ability to reduce DIDT. $(NH_4)_2SO_4$ precipitated preparations easily converted DIDT into ETU in the presence of NADH. CS_2 also formed. When DIDT and NADH were brought together with FAD or FMN, ETU formation was observed. Similarly, in phosphate buffer, DIDT reacted with L-cysteine, glutathione, or D-ascorbic acid to form ETU. A mechanism was proposed:



(Vonk and Sijpesteijn, 1976).

DIDT decomposed slowly to ETU in water (pH 7) with loss of CS_2. This reaction was stimulated by addition of: bacteria, yeast or filamentous fungi plus glucose; Pseudomonas fluorescens plus NADPH; cysteine, glutathione and ascorbic acid (Sijpesteijn and Vonk, 1974).

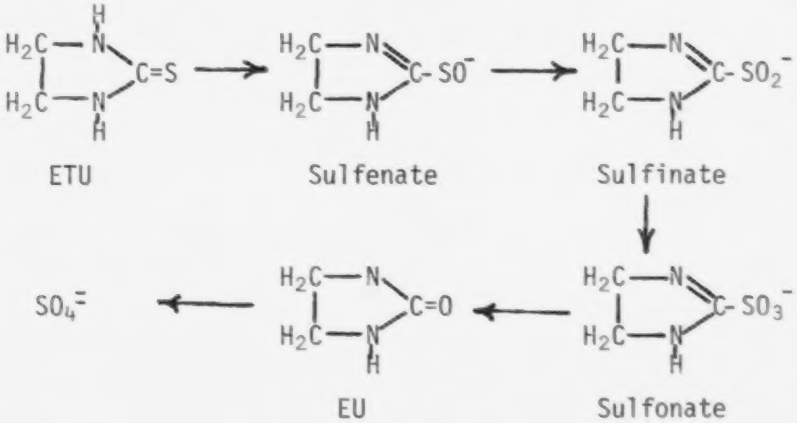
In studies of ETU oxidation, evidence indicated that in aqueous base oxidation by hypochlorite proceeded via sulfenate, sulfinate, sulfonate, and thence to EU and sulfate (Marshall and Singh, 1977).

Hypochlorite oxidized ethylene thiourea (ETU) to ethyleneurea (EU). The evidence suggested sequential oxidation in aqueous base via sulfenate, sulfinate, and sulfonate to sulfate plus EU. Hydrogen peroxide oxidation of ETU stopped at the sulfonate. Ethylene bisdithiocarbamates and ethylenethiuram monosulfide (ETM) were oxidized by hypochlorite to EU, CO_2 and sulfate (Marshall, 1977).

In agricultural uses, EBDC's are applied as aqueous suspensions. Decomposition begins almost immediately after dispersal in water. Decomposition products identified included ethylene bis(thiuram disulfide), ethylene bis(isothiocyanate), ETU, CS_2, COS, and CO_2 (Hylin et al., 1978).

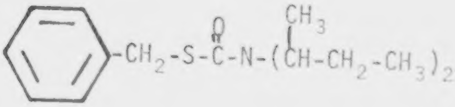
ETM was converted by post-microsomal rat liver supernatant to ETU. When ^{14}C-ETM was administered orally to male rats, almost 70% of the radioactivity was excreted in the urine. Urinary metabolites included ETU, EU, 4-imidazolin-2-one, and 2-imidazoline (Iverson et al., 1977).

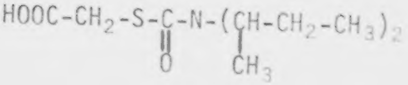
When ETU was administered to pregnant rats, analysis of collected urine showed the presence of three compounds. In addition to ETU, one other present was identified as ethyleneurea. A third was not identified. Plasma analysis showed the presence of ETU and another unidentified compound (Ruddick et al., 1976).



DREPAMON [*S*-Benzyl *N*,*N*-di-*sec*-butylthiolcarbamate]

The preemergent herbicide drepamon was applied to a simulated rice paddy. Drepamon was readily absorbed by rice and barnyard grass in the first stages of germination. Cochromatography of plant and water extracts indicated the presence of the following metabolites: di-*sec*-butylcarbamoylthiolglycolic acid (II); benzyl di-*sec*-butylcarbamoyl sulfoxide (III) and sulfone (IV); and dibenzyl disulfide (V). Analysis of soil indicated the presence of compound II as the major product present. Further tests indicated compound II did not form in the absence of microorganisms (Santi and Gozzo, 1976).





$$HOOC{-}CH_2{-}S{-}\underset{\underset{O}{\|}}{C}{-}N{-}(\underset{\underset{CH_3}{|}}{C}H{-}CH_2{-}CH_3)_2$$

II

DS-15647 [3,3-Dimethyl-1-methylthio-2-butanone O-(methylaminocarbonyl) oxime]

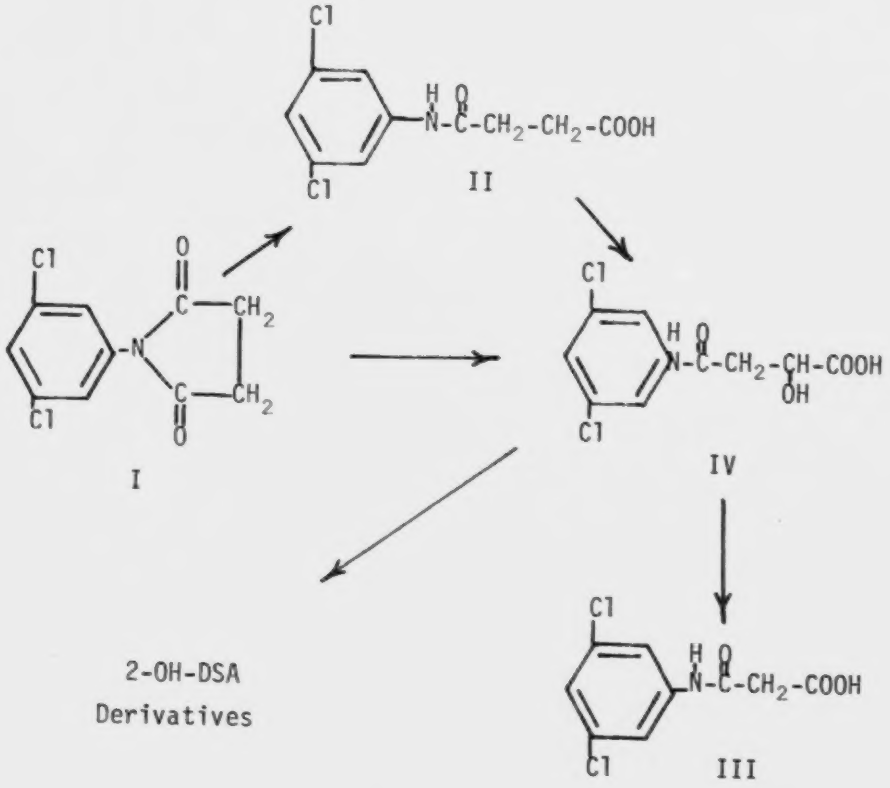
DS-15647 and its sulfone analog were administered to rats. DS-15647 was stepwise metabolized to the sulfoxide and sulfone. Conjugation, not identified, of the oxime-sulfone was significant. Other unidentified metabolites were also present. Subsequent to the sulfur oxidation, further degradation occurred with demethylation. Similar results were obtained with dogs (Tallant and Sullivan, 1974). When ^{14}C-N-methyl compounds were used, both gave rise to significant amounts (>30%) of $^{14}CO_2$, indicating N-methyl oxidation. When rats were administered the ^{14}C-S-methyl compounds, only a small amount (4%) appeared as $^{14}CO_2$ (Tallant et al., 1974).

DSI [*N*-(3',5'-Dichlorophenyl)succinimide]

DSI was adminstered orally to rats. Most of the dose was excreted readily and no difference between male and female rats was observed. When labeled material was used, no labeled residues were observed in tissues or organs after 24 h. In the collected urine, metabolites were identified by use of cochromatography and IR, or NMR and MS:

II. *N*-(3',5'-dichlorophenyl)succinamic acid (DSA)
III. *N*-(3',5'-dichlorophenyl)malonamic acid (DMA)
IV. *N*-(3',5'-dichlorophenyl)-2-hydroxysuccinamic acid (2-OH-DSA).

Derivatives of 2-OH-DSA were observed but not further identified. In dogs, these derivatives were also observed and were the main urinary metabolites. It was also found that the hepatic microsomes of rabbit liver were very active in degrading DSI to DSA. Liver homogenates of dog, mouse, and rat also degraded DSI but at a lower rate (Ohkawa et al., 1974a).



Cl
H O
N-C-CH2-CH2-COOH
Cl
II
Cl
O
C—CH2
N
C—CH2
O
Cl
I
Cl
H O
N-C-CH2-CH-COOH
OH
Cl
IV
2-OH-DSA
Derivatives
Cl
H O
N-C-CH2-COOH
Cl
III

EDIFENPHOS (Hinosan) [O-Ethyl S,S-diphenyl phosphorodithiolate]

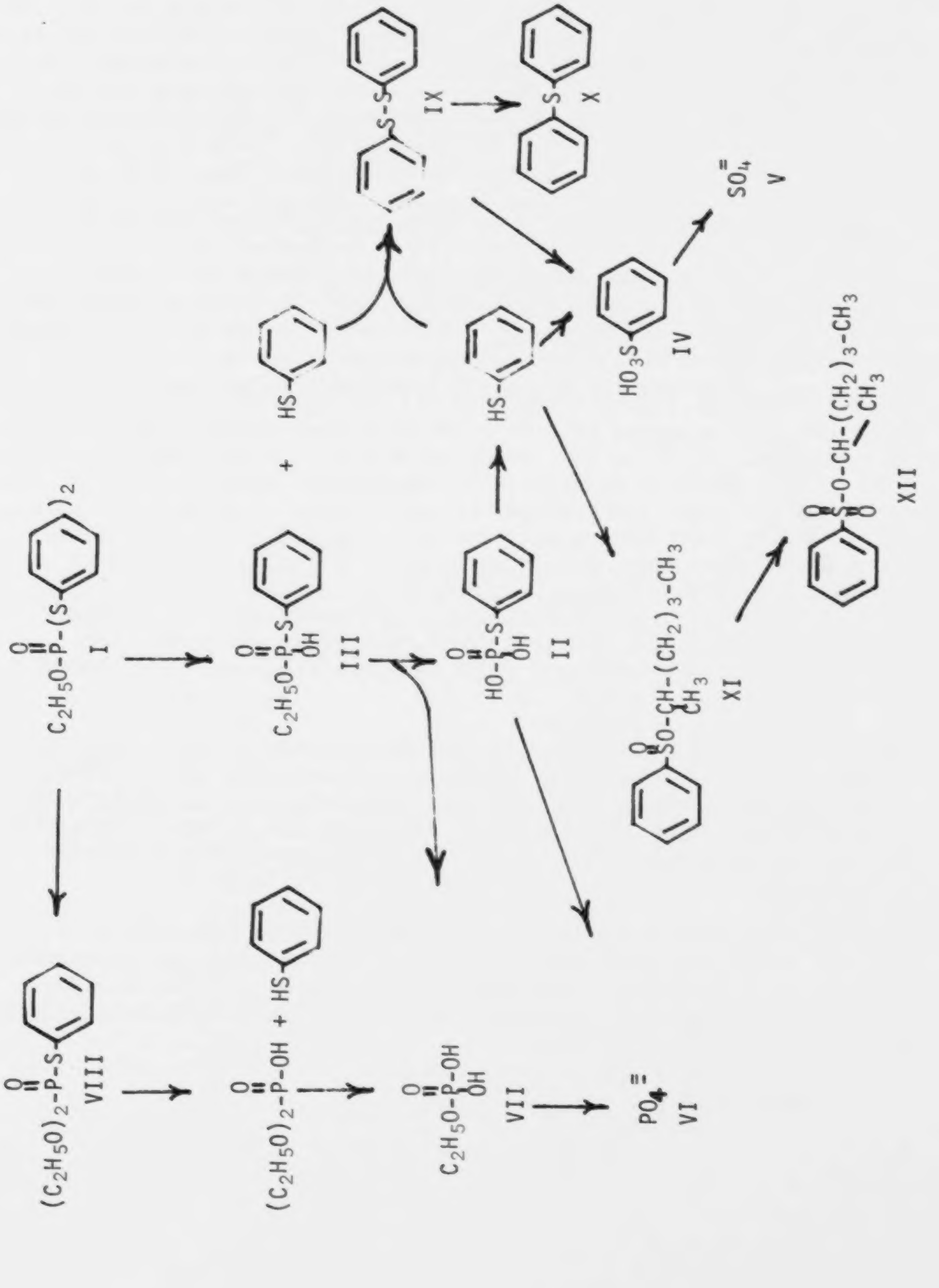
Following oral administration to rats and mice, edifenphos was rapidly absorbed, metabolized and excreted. Male and female showed no qualitative difference in metabolic pattern. Excretion via urine predominated. The same metabolites were observed in both species and in urine as well as feces. Those identified were (1) unchanged edifenphos, (2) diphenyl disulfide, (3) de-ethyl edifenphos, (4) O-ethyl-S-phenyl phosphorothiolate, and (5) phenylsulfate (Ueyama et al., 1978).

Edifenphos was applied to soil. Products observed and identified included: thiophenol; dibenzyl disulfide; benzenesulfonic acid; O-ethyl S-phenyl hydrogen phosphorothiolate; S-phenyl dihydrogen phosphorothiolate; S,S,S-triphenyl phosphorotrithiolate; S,S-diphenyl hydrogen phosphorodithiolate; O,O-diethyl S-phenyl phosphorothiolate; and sulfate (Tomizawa et al., 1976).

The photodecomposition of edifenphos (I) was studied under laboratory conditions with exposure to a UV light with wavelengths from about 295 to 400 nm. At 25 to 28C, exposure of a thin film of edifenphos to UV rapidly produced water-soluble compounds. When ^{35}S-labeled edifenphos was used, ion exchange chromatography revealed four radioactive spots. Co-chromatography and GLC showed that these products were S-phenyl dihydrogen phosphorothiolate (II), O-ethyl S-phenyl hydrogen phosphorothiolate (III), benzenesulfonate (IV), and sulfate (V). When the unlabeled photoproducts were methylated and analyzed by GLC, two peaks were observed and identified as the methylated products of phosphate (VI) and ethyl hydrogen phosphate (VII) (Murai, 1977 and 1978).

When an aqueous solution of edifenphos was exposed to UV, in addition to compounds II-VII, two other products were observed but not identified. Further irradiation of these two compounds after methylation produced methyl esters of benzenesulfonic acid and sulfate, indicating that the unknowns were intermediates in the oxidation of phenylthio to benzenesulfonate and sulfate (Murai, 1977 and 1978).

In hexane, the photoproducts of edifenphos included compounds II-VII, as well as several new ones identified as O,O-diethyl S-phenyl phosphorothiolate (VIII), diphenyl disulfide (IX), diphenyl sulfide (X), 1-methylpentyl benzenesulfinate (XI), and 1-methylpentyl benzenesulfonate (XII) (Murai, 1977 and 1978).


C2H5O-P(=O)-(S-C6H5)2
I
C2H5O-P(=O)(OH)-S-C6H5
III
HO-P(=O)(OH)-S-C6H5
II
HS-C6H5 + HS-C6H5
C6H5-S-S-C6H5
IX
C6H5-S-C6H5
X
HS-C6H5
HO3S-C6H5
IV
SO4=
V
C6H5-SO-O-CH(CH3)-(CH2)3-CH3
XI
C6H5-SO2-O-CH(CH3)-(CH2)3-CH3
XII
(C2H5O)2-P(=O)-S-C6H5
VIII
(C2H5O)2-P(=O)-OH + HS-C6H5
C2H5O-P(=O)(OH)-OH
VII
PO4≡
VI

ENDOSULFAN (Thiodan) [6,7,8,9,10,10-Hexachloro-1,5,5a,6,9,9a-hexahydro-6,9-methane-2,4,3-benzodioxathiepine-3-oxide]

α-Endosulfan = Endosulfan I
β-Endosulfan = Endosulfan II

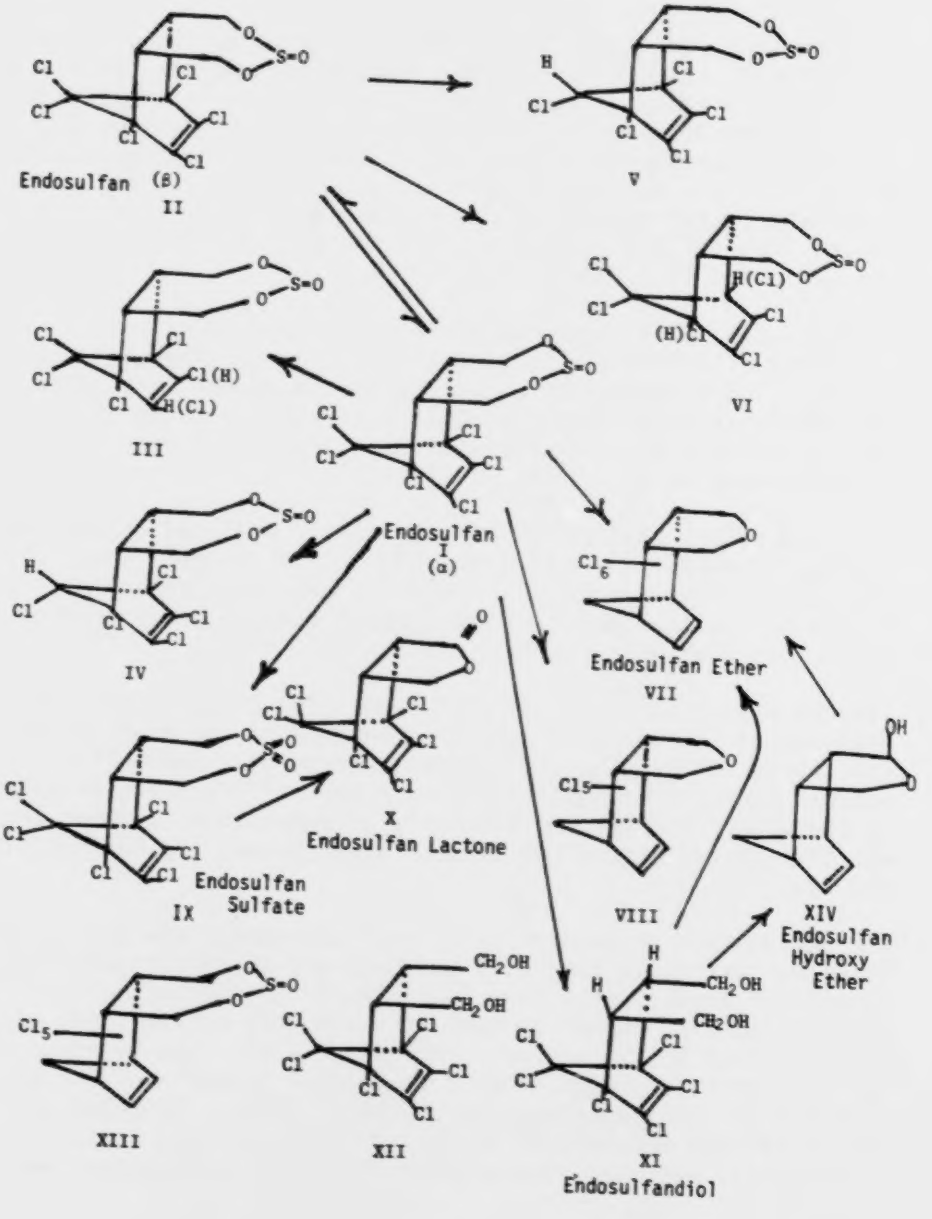
In the mouse, the major metabolite of endosulfan was excreted in feces and urine as endosulfan lactone. Endosulfan and its sulfate were not observed in muscle, kidney, liver, and fat after 10 days' administration of the parent compound or its sulfate. In an ecosystem, all food chain organisms interconverted both endosulfan isomers and particularly metabolized the α-isomer to its sulfate. After picking up endosulfan from water, high amounts of the sulfate were concentrated by fish and snail. More of the sulfate was concentrated by fish when exposed to the α-isomer (Ali, 1978).

α- and β-Endosulfan were administered to rats. Analyses of feces, urine and bile showed no significant differences between the two isomers. Both isomers produced similar residues: endosulfan diol, the α-hydroxy ether and endosulfan lactone were found in feces, urine and bile; endosulfan sulfate and endosulfan ether were found in feces only (Dorough et al., 1978).

When endosulfan was applied to pear trees, analyses showed that the β-endosulfan was more persistent than the α-isomer. About 75% of the α-endosulfan was gone in the first week post treatment. Endosulfan sulfate was observed and reached maximum concentration 2-4 weeks post treatment (MacNeil and Hikichi, 1976).

Tobacco plants were treated with endosulfan I and II and the sulfate. Analyses of the leaves showed the presence of the diol, ether and lactone in addition to the original compounds. Endosulfan II, however, was not found in leaves treated with the sulfate. The principal product in the green leaf was small amounts of endosulfan I. When the leaf was flue-cured, endosulfan II was found (Chopra and Mahfouz, 1977a and b).

The degradation of endosulfan by soil microorganisms was studied. Of those tested, 16 fungi, 15 bacteria and three actinomycetes were capable of metabolizing more than 30% of applied endosulfan. The major metabolite formed by most of the highly active fungi was the sulfate; most active bacteria formed the diol. The hydroxyether, two unidentified products and a very small amount of $^{14}CO_2$ was also formed from labeled endosulfan (Martens, 1976). In other soil studies, endosulfan was metabolized to the sulfate, diol and lactone. When flooded soil was used, the sulfate, diol and hydroxyether were


Cl
Cl
Cl
Cl
Cl
Cl
O
S=O
O
Endosulfan (β)
II
H
Cl
Cl
Cl
Cl
Cl
O
S=O
O
V
Cl
Cl
H(Cl)
(H)Cl
Cl
Cl
O
S=O
O
VI
Cl
Cl
Cl
Cl(H)
Cl
H(Cl)
O
S=O
O
III
Cl
Cl
Cl
Cl
Cl
Cl
O
S=O
O
Endosulfan
I
(α)
H
Cl
Cl
Cl
Cl
Cl
O
S=O
O
IV
Cl_6
O
Endosulfan Ether
VII
Cl
Cl
Cl
Cl
Cl
Cl
O
O
X
Endosulfan Lactone
Cl
Cl
Cl
Cl
Cl
Cl
O
S
O
O
O
Endosulfan
Sulfate
IX
Cl5
O
VIII
OH
O
XIV
Endosulfan
Hydroxy
Ether
Cl_5
O
S=O
O
XIII
CH_2OH
CH_2OH
Cl
Cl
Cl
Cl
Cl
Cl
XII
H
H
CH_2OH
CH_2OH
Cl
Cl
Cl
Cl
Cl
Cl
XI
Endosulfandiol

observed (Martens, 1977). In other studies, endosulfan initially was slowly converted to the sulfate and then disappeared rapidly after a lag of about 120 days (Van Dyk and Van Der Linde, 1976).

Endosulfan I pyrolysis at 880-900C produced the following compounds:

endosulfan II
endosulfan ether
hexachlorocyclopentadiene
methyl chloride
dichloromethane
chloroform
1,1-dichloroethylene
1,1-dichloroethane
trichloroethylene
tetrachloroethylene
chlorobenzenes
carbon tetrachloride

(Chopra et al., 1978)

ENDOTHALL [7-Oxabicyclo-(2.2.1)heptane-2,3-dicarboxylic acid]

About .72% of endothall added to a simulated impoundment persisted for 30 days. During this period, there was a weedkill followed by oxygen depletion. When the oxygen was restored, endothall disappearance was rapid (Simsiman and Chesters, 1975).

ENP [1,1-Bis-(p-ethoxyphenyl)-2-nitropropane]

Rats fed ENP (I) excreted into the urine the following metabolites:

II. 1-(p-ethoxyphenyl)-1-(p-hydroxyphenyl)-2-nitropropane
III. 1,1-bis(p-hydroxyphenyl)-2-nitropropane
IV. 1,1-bis(p-hydroxyphenyl)-2-propanone
V. 1,1-bis(p-hydroxyphenyl)-2-hydroxypropane.

(Ciba-Gergy, 1976)

ENP was topically applied to 4-day old adult flies from a Rothamsted resistant strain. Metabolites identifies in fractions from the house flies included 1-(p-ethoxyphenyl)-1-(p-hydroxyphenyl)-2-nitropropane and 1,1-bis(p-hydroxyphenyl)-2-nitropropane. In similar studies with the cluster caterpillar (Spodoptera litura), one compound was tentatively identifies as 1,1-bis(p-hydroxyphenyl)-2-propanone (Morton et al., 1976).

EP-475 [Ethyl m-hydroxycarbanilate carbanilate]

PHENMEDIPHAM [Methyl m-hydroxycarbanilate m-methylcarbanilate]

When administered to rats, both compounds were metabolized rapidly and eliminated. EP-475 and phenmedipham were hydrolyzed to ethyl and methyl N-(3-hydroxyphenyl)carbamate, respectively. Both were then metabolized to m-aminophenol, which N-acetylated. The hydroxyphenyls were metabolized to glucuronides and sulfates. The major metabolites formed by hepatic preparations were the hydroxyphenylcarbamates. These were also formed by human, chicken, cow, and rat blood plasma (Sonawane, 1972).

When exposed to UV (254 and 364 nm), these two compounds were converted primarily to the hydroxyphenylcarbamates. In alkaline soil, phenmedipham was decomposed to the hydroxyphenylcarbamate. This in turn was converted to the m-aminophenol, which was adsorbed and complexed (Sonawane, 1972).

EPN [*O*-Ethyl *O*-(*p*-nitrophenyl)phenylphosphonothioate]

After administration of EPN to male Sprague-Dawley rats, analysis of urine indicated the presence of *p*-nitrophenol (Bradway et al., 1977).

Inhibition studies conducted with the two isomers of EPN oxon indicated that the inhibition of α-chymotrypsin was reversed with PAM at almost equal rates for the two isomers. This was interpreted to mean that the P-O-serine bond underwent simple hydrolysis in the reactivation process (Ohkawa et al., 1978c).

EPRONAZ [1-(N-Ethyl-N-propylcarbamoyl)-3-propylsulfonyl-1,2,4-triazole]

The rate of hydrolysis of epronaz was determined at varying temperatures and pH. The rate increased as alkalinity and temperature increased, varying from 20.8 h to 0.73 h (70C and pH 6.3 and 73C and pH 8.1, respectively) to 800 h and 31.5 h at 40C and pH 6.3 and 42C and pH 8.1, respectively (Brookes and Copping, 1975).

ETHEPHON (CEPA, Ethrel, Camposan) [2-Choroethylphosphonic acid]

In rye, ethephon was metabolized to ethylene and CO_2 (Boguszewski and Schutte, 1978).

In suspension cultures of Hevea brasiliensis, ethephon was metabolized to a number of compounds. One chromatographed similarly to 2-hydroxyethylphosphonic acid (Audley and Wilson, 1978).

After application of ^{14}C-ethephon to young Hevea brasiliensis seedlings, analysis indicated the presence of labeled materials, in addition to ethephon, in extracts of tissues as late as 15 days post treatment. Chromatography of aqueous extracts from leaves indicated the presence of at least 11 compounds. One was identified as 2-hydroxyethylphosphonic acid (2-HEPA) (Audley et al., 1976).

After application of ^{14}C-ethephon to olive trees, the only metabolite detected was ^{14}C-ethylene (Epstein et al., 1977).

When mature 'Bearss' lemon fruit was treated with ^{14}C-labeled-ethephon, ^{14}C-ethylene formed in large amounts within 2 days (Young and Jahn, 1975).

After application of ^{14}C-ethephon to tomato, cucumber and squash plants, conversion of ethephon to ^{14}C-ethylene was observed during the first day--about 21% by squash and 10-15% by tomatoes. Some $^{14}CO_2$ was formed subsequently. In the squash seedling, much of the ^{14}C was present as a metabolite whereas in tomatoes it was present as ^{14}C-ethephon (Yamaguchi et al., 1971).

After application of labeled ethephon to grapes, indications of a metabolite were observed but it was not identified (Weaver et al., 1972).

Ethephon was applied to peach fruits. Results of the studies indicated that the ethephon was actively degraded in young fruit but only slowly in older peach fruits (Lavee and Martin, 1974a). Methanol extracts of the treated peach fruits contained unchanged ethephon plus four metabolites. At least one of these was a sugar conjugate (Lavee and Martin, 1974b).

When ^{14}C-ethephon was addead to leaf discs of tobacco (Nicotiana tabacum) labeled ethylene, but not $^{14}CO_2$, evolved (Domir, 1975; Domir and Foy, 1975 and 1978a and b).

In Calimyrna fig, ^{14}C-ethephon was converted to ^{14}C-ethylene in 4 days. Some $^{14}CO_2$ was also formed (Puech, 1974).

ETHION [O,O,O',O'-Tetraethyl S,S'-methylene bisphosphorodithioate]

Turkeys were confined in pens on soil that was sprayed with ethion. In residue analyses of fat and skin, the only metabolite detected was ethion monooxon. This occurred at low levels in skin of birds in pens treated at the upper level of 40 lb AI/acre (Ivey et al., 1975).

ETHOFUMESATE [(±)2-Ethoxy-2,3-dihydro-3,3-dimethylbenzofuran-5-yl-methansulfonate]

Persistence of ethofumesate in soil was temperature dependent, indicating that it was dependent on the action of soil microorganisms. In sandy loam and loam soils, the time for dissipation of 50% of applied herbicide was 7.7 and 12.6 weeks, respectively (Schweizer, 1976).

After application to soil, ethofumesate and metabolites were absorbed by the roots of sugar beets and translocated to the foliage (Eshel et al., 1978).

ETHOPROPHOS (Ethoprop) [O-Ethyl S,S-dipropyl phosphorodithioate]

Persistence of ethoprophos in soil was found to approximate first order kinetics. In humic sand (pH 4.5) and peaty sand (pH 4.6), the half-life was 87 days. The half-life ranged between 14 and 28 days in sandy loam (pH 7.2) and a loam soil (pH 7.3) (Smelt et al., 1977).

ETHYLTHIOMETON (Disulfoton, Di-syston) [O,O-Diethyl S-(2-ethylthioethyl)phosphorodithioate]

When ethylthiometon was added to soil under paddy conditions, there was rapid oxidation to the corresponding sulfoxide and sulfone. In silt loam soil, under paddy conditions, reduction of the sulfoxide to ethylthiometon occurred. At 28C, the half-life of ethylthiometon and its five metabolites was about 50 days (Takase and Nakamura, 1974).

Disulfoton was applied to strawberries for aphid control. Residues contained traces of the sulfoxide, sulfone, and oxygen analog of the sulfone of disulfoton. Measurable residues of these compounds were also present in the soil 2 years after application (Chisholm and Specht, 1978).

Disulfoton was incubated with various soils. A number of products were formed but only disulfoton sulfone persisted in soil (Clapp, 1974). The fate of disulfoton in Portneuf silt loam soil was studied. Oxidation of this compound to the sulfoxide and sulfone was observed. The half-life of disulfoton was approximately 2 days but varied somewhat with temperature and moisture. Disulfoton sulfone persisted for more than 64 days; the disulfoton and its sulfoxide, 32 days or less. The corresponding oxygen analogs of the metabolites were not observed (Clapp et al., 1976).

ETO [Ethylene oxide]

After fumigation of coca powder with ETO, several derivatives were isolated. Using IR and MS, these compounds have been identified as N,N-bis-(di-ethoxy-O-hydroxyethyl)isoleucylalanyl-cysteine, and N-(ethoxy-O-hydroxyethyl)tyrosine (Pfeilsticker and Siddiqui, 1976).

ETRIMFOS [*O*,*O*-Dimethyl *O*-(6-ethoxy-2-ethyl-4-pyrimidinyl)phosphorothioate

When etrimfos was administered to rats, most of the material was excreted in the urine. Five compounds, free and conjugated, were observed: 6-ethoxy-2-ethyl-4-hydroxypyrimidine; 2-ethyl-4,6-dihydroxypyrimidine; 6-ethoxy-4-hydroxy-2-(1-hydroxyethyl)pyrimidine; 6-ethoxy-4-hydroxy-2-(2-hydroxyethoxy)pyrimidine; and 2-ethyl-4-hydroxy-6-(2-hydroxyethoxy)pyrimidine. In urine of goats administered etrimfos, only the first three compounds above were observed (Karapally and Madrid, 1978).

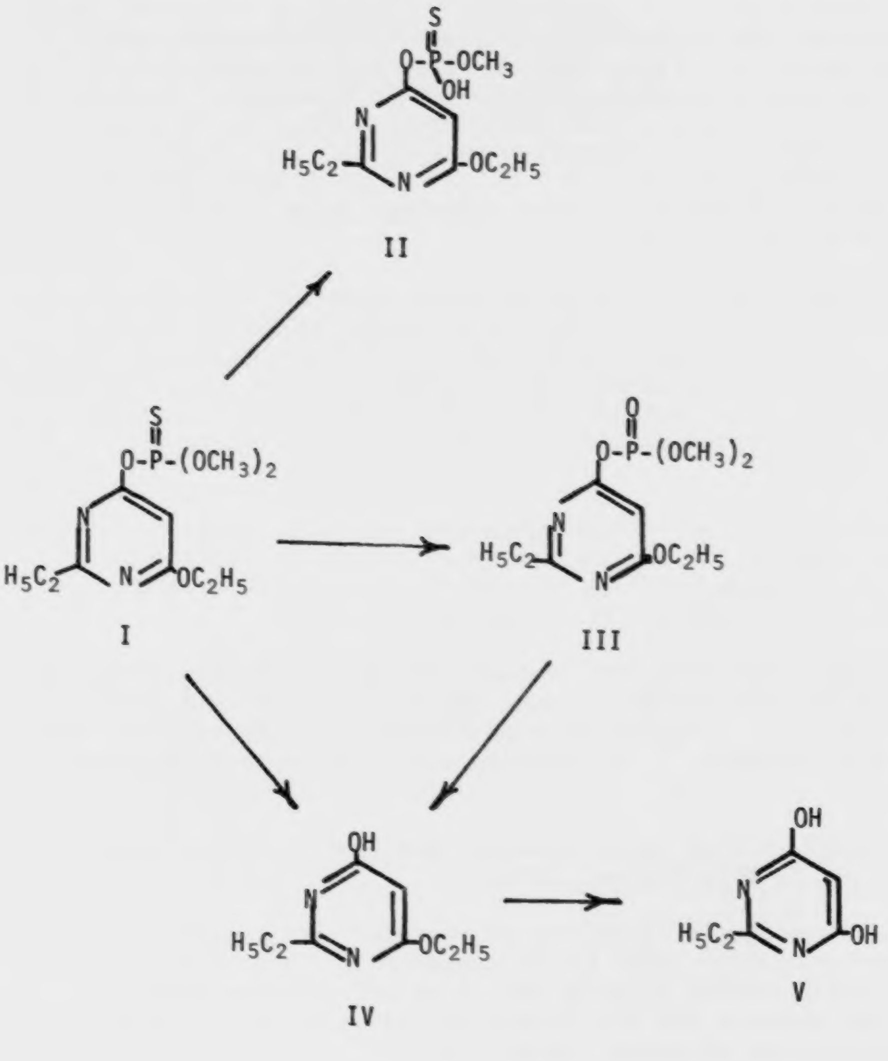
With liver preparations from mice and rats, desmethyl etrimfos (II) predominated when 10800g supernatant and 100000g soluble fractions were used. With microsomes, the pyrimidinol (IV) predominated. Brain homogenates only produced the desmethyl etrimfos. Glutathione transferases and, to a lesser extent, mixed-function oxidases were responsible for etrimfos metabolism (Ioannou, 1978; Ioannou and Dauterman, 1978).

In the development of analytical procedures for this compound, corn was treated with etrimfos and weathered in the field. Analyses indicated the presence of unreacted etrimfos (I), the *O*-analog (III), and the hydrolysis product (IV) (Bowman et al., 1978)

Twenty-one days after treatment of bean and corn seedlings, unreacted etrimfos was the main residue. Small amounts of 6-ethoxy-2-ethyl-4-pyrimidinol (IV), 2-ethyl-4,6-pyrimidinediol (V), the etrimfos oxon (II), and four unidentified metabolites were also present (Akram et al., 1978).

Enzyme preparations from corn, soybeans, and lima beans did cause dearylation of etrimfos (Ioannu, 1978).

Preparations from housefly abdomens of resistant and susceptible strains demethylated etrimfos in the presence of glutathione transferase and added reduced glutathione. A potent cholinesterase inhibitor was observed but not identified but no oxidative dearylation of etrimfos was observed (Ioannu, 1978).


S
O-P-OCH3
OH
N
H5C2
N
OC2H5
II
S
O-P-(OCH3)2
N
H5C2
N
OC2H5
I
O
O-P-(OCH3)2
N
H5C2
N
OC2H5
III
OH
N
H5C2
N
OC2H5
IV
OH
N
H5C2
N
OH
V

FAMPHUR (Famophos, Warbex) [O,O-Dimethyl O-p-(N,N-dimethylsulfamoyl) phenyl phosphorothioate]

Famphur was injected into muscle of reindeer. Residue levels, except at the sight of injection, were very low after the first day. Residues consisted of famphur and its oxon, the latter generally present at levels below 1 ppm. These compounds were detectable for 4.5 days in liver; 12 days in kidney; 12 days in shoulder muscle. After 20 days, a residue was found only at site of injection in shoulder muscle (Erne and Nordkvist, 1970).

FB (Voronit, Neovoronit) [2-(2-Furyl)benzimidazole]

FB was administered to horses, goats, dogs, rabbits and rats. Urine was collected and analyzed after extraction, purification by liquid-liquid partitioning, TLC and column chromatography. UV absorption, IR, NMR, MS, chemical and enzymatic reactions and syntheses were used to identify four of the seven metabolites observed: (S)-(-)-4-(2-benzimidazolyl)-4-hydroxybutyric acid (II), 2-(2-furyl)-5(6)-hydroxybenzimidazole (III), and its β-D-glucuronide (IV) and sulfate (V). Qualitative and quantitative differences in the metabolism of FB were observed in the test animals. Qualitative results are tabulated.

Animal	Metabolites Found in Urine
Horse	II, III, IV, V and one unidentified compound.
Goat	II, III, IV, V and three unidentified compounds.
Dog	II, IV, V and three unidentified compounds.
Rabbit	II, IV, V and two unidentified compounds.
Rat	II, III, IV, V and three unidentified compounds.

(Frank, 1971).

FCA [2,5-Dimethylfuran-3-carboxanilide]

A Nocardia sp., capable of using acid anilides as a sole source of carbon, was isolated from soil. Degradation was initiated by amide hydrolysis. This was followed by oxidation of the aniline moiety via pyrocatechol and the β-ketoadipate pathway. The acid moiety accumulated in the incubation medium (Bachofer, 1976).

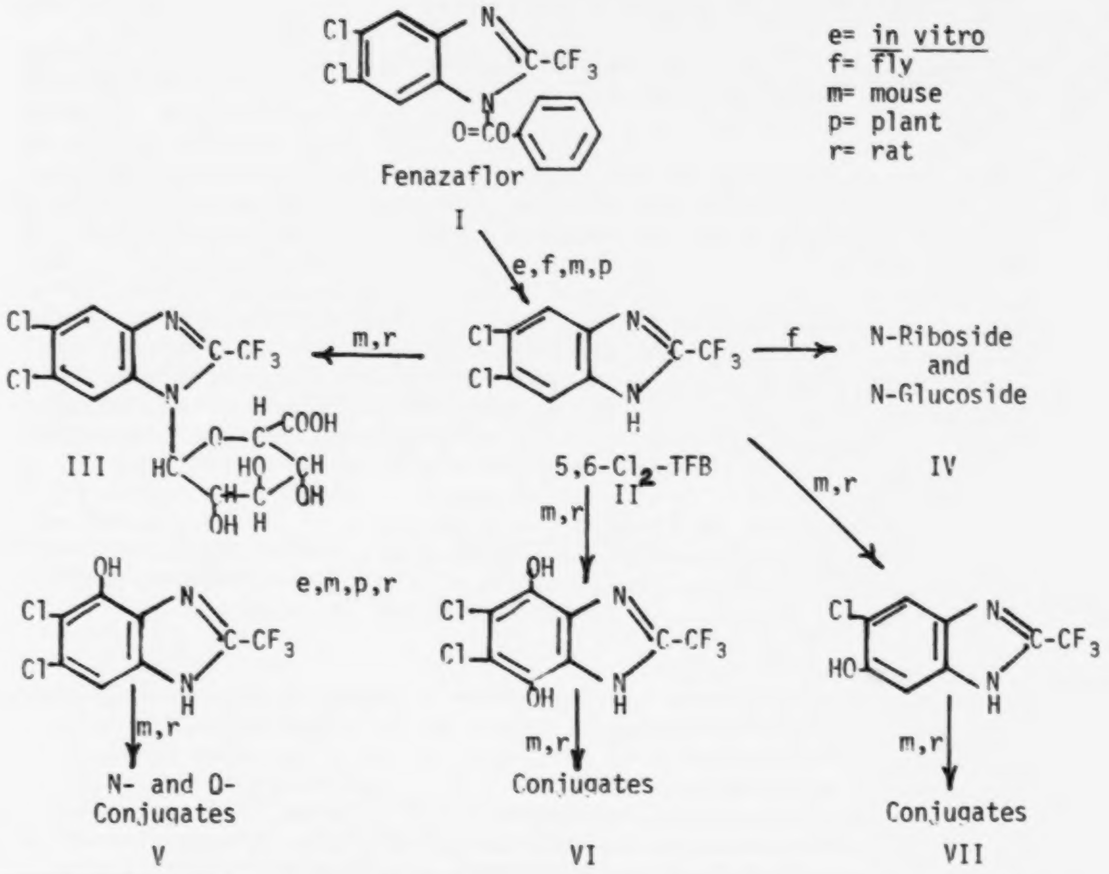
FENAZAFLOR [5,6-Dichloro-1-phenoxycarbonyl-2-trifluoromethylbenzimidazole]

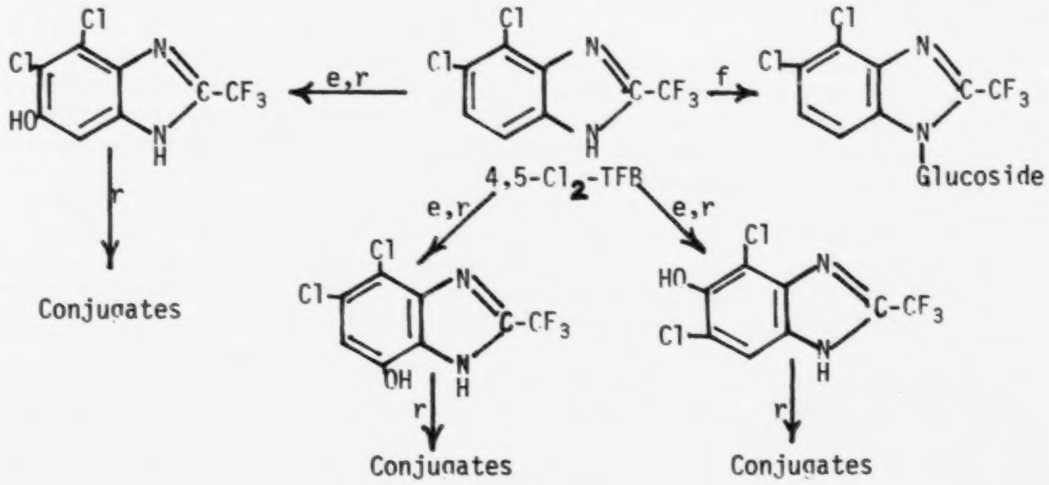
^{14}C-Fenazaflor in DMSO was orally administered to male albino Swiss-Webster mice. Analysis of collected urine revealed the presence of: 5,6-Cl_2-TFB (II); conjugates of 5-Cl-6-HO-TFB (VII); N-glucuronide TFB (III); 4-HO-5,6-Cl_2-TFB conjugate (V); 4,7-$(HO)_2$-5,6-Cl_2-TFB conjugate (VI); N-glucoside TFB (IV); and N-riboside TFB. Other conjugates were not identified (Bowker and Casida, 1969).

Thirteen days after application of fenazaflor to foliage of bean plants, about 99% of the residue was unchanged fenazaflor. Some 5,6-Cl_2-TFB formed within 6 days after injection; and, after 28 days, more than 99% of the label was as 5,6-Cl_2-TFB. After treatment of apple fruit and foliage with fenazaflor, metabolites included 5,6-Cl_2-TFB, N-glucoside of 4-OH-5,6-Cl_2-TFB, 4-O-glucoside of 5,6-Cl_2-TFB, and some unidentified compounds (Bowker and Casida, 1969).

In apples from field trials of fenazaflor, 5,6-Cl_2-TFB and 4-OH-5,6-Cl_2-TFB glucoside were detected. Trifluoroacetic acid was also found as a tightly bound form in apples (Crofts et al., 1972). When fenazaflor was applied to soil, 5,6-Cl_2-TFB was observed (Whiteoak et al., 1973).

A liver microsome system converted 4,5-Cl_2-TFB to 6-OH- and 7-OH-4,5-Cl_2-TFB and some 4,6-Cl_2-5-OH-TFB. When 5,6-Cl_2-TFB was used, only 4-OH-5,6-Cl_2-TFB was identified. When mice and rats were administered 5,6-Cl_2-TFB, the metabolites identified were the same as observed with fenazaflor. After administration of 4,5-Cl_2-TFB to rats, metabolites observed were a conjugate of 4,5-Cl_2-6-OH-TFB, and other conjugates not identified but believed to include 4,5-Cl_2-7-OH-TFB; 4,5-Cl_2-6-OH-TFB; and 4,6-Cl_2-5-OH-TFB. When injected into houseflies, 4,5-Cl_2-TFB and 5,6-Cl_2-TFB give rise to respective N-glucosides, probably N-glucoside-6-phosphates (Bowker and Casida, 1969).


e= in vitro
f= fly
m= mouse
p= plant
r= rat
Cl
Cl
N
C-CF3
N
O=CO
Fenazaflor
I
e,f,m,p
m,r
f
N-Riboside
and
N-Glucoside
IV
5,6-Cl2-TFB
II
III
COOH
m,r
e,m,p,r
m,r
N- and O-
Conjugates
V
m,r
Conjugates
VI
m,r
Conjugates
VII


e,r
f
4,5-Cl2-TFB
Glucoside
r
Conjugates
e,r
e,r
r
Conjugates
r
Conjugates

FENITROTHION (Sumithion, Folithion) [O,O-Dimethyl O-(3-methyl-4-nitrophenyl)phosphorothioate]

S-METHYL FENITROTHION [O,S-Dimethyl O-(3-methyl-4-nitrophenyl) phosphorothiolate]

A glutathione-dependent enzyme preparation was made from rat livers and incubated with fenitrothion. The main product was desmethylfenitrothion. Methylglutathione probably formed also (Davidek and Seifert, 1975).

Mouse liver enzyme degraded fenitrothion to desmethylated metabolites, the oxon analog, nitrocresol and 5-hydroxy-2-nitrobenzoic acid. The latter metabolite was also produced by liver microsomal preparations from guinea pigs and rats (Douch et al., 1968). Rat liver MFO metabolized fenitrothion to the oxon. The oxon 3-methyl group was converted to a carboxylic acid (Miyamoto and Ohkawa, 1978).

In rats treated with fenitrothion, 4-nitro-m-cresol (PNMC) was excreted in urine (Osicka-Koprowska et al., 1978). Male Wistar rats with hepatic lesions were administered fenitrothion. In vivo detoxication was not affected by the lesions. Metabolites observed included:

Desmethylfenitrothion
Desmethylfenitrooxon
Desmethylaminofenitrothion
3-Methyl-4-nitrophenol
3-Methyl-4-nitrophenyl sulfate
3-Methyl-4-nitrophenyl β-glucuronide
3-Methyl-4-aminophenyl sulfate
3-Hydroxymethyl-4-nitrophenol
3-Carboxy-4-nitrophenol

(Miyamoto et al., 1977b and 1978)

In a comparative study, m-methyl-^{14}C-fenitrothion was administered orally to dogs, rats, mice and rabbits. Radiocarbon was eliminated rapidly and mainly into the urine. Results of these studies are summarized in the following table.

Metabolite	Rat	Mice	Rabbit	Dog
	Species			
Fenitrooxon			+	
Desmethylfenitrooxon	++++	++++	+	+
Desmethylfenitrothion	++	++++	++	+++++
Aminofenitrothion			+	
Desmethylaminofenitrothion	+		+	
3-Methyl-4-nitrophenol	++	++++	+++	++
3-Methyl-4-nitrophenyl glucuronide	++	++	+++	+
3-Methyl-4-nitrophenyl sulfate	+++++	++++	+++++	++
3-Methyl-4-aminophenyl sulfate	+		+	
3-Methyl-4-formylaminophenol	+		+	
3-Methyl-4-formylaminophenyl glucuronide	+		++	+
3-Methyl-4-acetylaminophenol	+			
3-Hydroxymethyl-4-acetylaminophenol	++		+	+
5-Hydroxy-2-nitrobenzyl alcohol	+			+
5-Hydroxy-2-nitrobenzoic acid	+		+	
O,O-Dimethyl O-(3-CO$_2$H-4-NO-phenyl)phosphorate	+			
O,O-Dimethyl O-(4-Acetyl NH-3-CH$_2$OH-phenyl) phosphorate	+			

(Miyamoto et al., 1976)

When administered to goats, fenitrothion was rapidly metabolized; and, one day after treatment, no unchanged fenitrothion remained. The metabolites observed in urine, feces and milk included aminofenitrothion; O-methyl-O-hydrogen O-(3-methyl-4-acetylaminophenyl)phosphate; O,O-dimethyl O-(3-methyl-4-sulfoaminophenyl)phosphorothioate (N-sulfoaminofenitrothion); formylaminofenitrothion; acetylaminofenitrothion; 3-methyl-4-acetylaminophenol; aminofenitrooxon; formylaminofenitrooxon; acetylaminofenitrooxon; N-sulfo aminofenitrooxon; desmethylaminofenitrothion; and desmethylacetylaminofenitrooxon (Mihara et al., 1978).

S-Methyl fenitrothion and fenitrooxon stability was investigated. Results indicated that there were no significant differences between I_{50} values for the two compounds when tested with mammalian plasma pseudocholinesterase or bovine erythrocyte acetylcholinesterase with the exception of the human. At pH 7.4, spontaneous hydrolysis of the S-methyl isomer was more rapid than that of fenitrooxon. The rate of hydrolysis for the S-methyl analog by rat livers was 25-fold higher than was observed with fenitrooxon (Myatt et al., 1975). Excretion of PNMC in the urine of rats was more rapid and the amounts larger from the S-methyl isomer than from fenitrothion (Rosival et al., 1976).

White pine, white spruce, and yellow birch seeds were incubated with purified fenitrothion in petri dishes. Most of the insecticide was located in the embryo of the seed. In all three species, the oxon and S-methyl analog were detected. Neither compound was found in the aqueous solution in which the seeds were germinated. Desmethylfenitrothion was observed in the seeds of all three species. The formation of S-methyl glutathione was also observed. Other studies indicated that S-methyl fenitrothion was formed through the alkylation of desmethyl fenitrothion by fenitrothion. 3-Methyl-4-nitrophenol was detected by GC and TLC. Metabolic pathways involving hydrolysis of fenitrothion, the S-methyl analog, and the oxon were suggested (Hallett et al., 1975 and 1977).

^{14}C-m-Methyl-labeled fenitrothion was applied to rice grains at 6 and 15 ppm and stored for 12 months at 15C and 30C. Decomposition was greater at 30C and the half-life was about 4 months and more than 12 months, respectively, at the two temperatures. In addition to desmethylfenitrothion and 3-methyl-4-nitrophenol, the following compounds were also observed:

fenitrothion S-isomer
fenitrooxon
desmethylfenitrothion S-isomer
desmethylfenitrooxon
3-hydroxymethyl-4-nitrophenol
1-methoxy-3-methyl-4-nitrobenzene
1,2-dihydroxy-4-methyl-5-nitrobenzene
1,2-dimethoxy-4-methyl-5-nitrobenzene
an unidentified conjugate of 3-methyl-4-nitrophenol

When unpolished rice grains were cooked with fenitrothion, the primary decomposition products were desmethylated derivatives and 3-methyl-4-nitrophenol (Takimoto et al., 1978).

After aerial deposition of an aqueous fenitrothion formulation, water samples were taken. Residues were greater in surface waters initially than found in subsurface waters. GC analyses indicated the presence of aminofenitrothion and possibly traces of demethyl aminofenitrothion. S-Methyl fenitrothion was detected in surface waters for up to 10 h post spray. It was also found in the formulation (Moody et al., 1978).

Fenitrothion was applied to model aquatic ecosystems, using ^{14}C-ring- and ^{14}C-methoxy-labeled fenitrothion. After 7 days, more than 30% of the initial material was found in the mud in the form of aminofenitrothion. In the water, exposed to light, the major products were dimethyl phosphorothioate, desmethyl fenitrothion, and carboxyfenitrothion. Plant bioaccumulation of fenitrothion showed species variation and was in the range of 300-1000-fold. Under lighted conditions only, a metabolite was observed and tentatively identified as desmethyl fenitrothion aldehyde (Weinberger et al., 1978).

In fish, fenitrothion was metabolized by P=S oxidation, cleavage of P-O-aryl bond and O-demethylation. The phenol formed was conjugated with glucuronic acid (Miyamoto, 1976). Fenitrothion was readily taken up by rainbow trout and southern top-mouthed minnows. Rainbow trout metabolized fenitrothion to the oxon, desmethyl oxon, desmethyl fenitrothion, and 3-methyl-4-nitrophenol and its glucuronide (Takimoto and Miyamoto, 1976).

In forest soils, fenitrothion degradation was 50% after 5 days. After 50 days, fenitrothion degradation yielded CO_2, 3-methyl-4-nitrophenol, 3-methyl-4-nitroanisole, and radiocarbon bound to humin, humic acid and fulvic acid (Spillner et al., 1978).

^{14}C-Fenitrothion labeled at the m-methyl group was added to soils. Depending on the soil, under upland conditions, fenitrothion $t_{1/2}$ = 12 to 28 days. In addition to the major products which were identified as 3-methyl-4-nitrophenol and $^{14}CO_2$, traces of aminofenitrothion, formylaminofenitrothion, and acetylaminofenitrothion were observed. Water-soluble compounds were not identified. The $^{14}CO_2$ formed after about 60 days. In flooded soil, degradation was more rapid and the main product was aminofenitrothion. 3-Methyl-4-nitrophenol, $^{14}CO_2$, formylaminofenitrothion, and acetylaminofenitrothion were also observed (Takimoto et al., 1976).

When fenitrothion was incubated with fungi (Fusarium sp.) or bacteria (Bacillus sp.), the major product was aminofenitrothion. The minor metabolites identified included 3-methyl-4-nitrophenol, desmethylfenitrothion, 3-methyl-4-aminophenol, formylaminofenitrothion, and acetylaminofenitrothion (Takimoto et al., 1976).

Fenitrothion was exposed to UV irradiation. Disappearance followed first-order kinetics. In hexane, the $t_{1/2}$ was 85 minutes. The main product was the oxon. Other compounds identified by GC-MS and NMR included S-methyl fenitrothion, denitrofenitrothion, and formylfenitrothion. Irradiation in methanol produced carbomethoxyfenitrothion primarily plus carboxyfenitrothion, 4-nitro-m-cresol, S-methylfenitrothion and traces of the oxon. With acetone as the reaction medium, 4-nitro-m-cresol, carbomethoxyfenitrothion and carbomethoxyfenitrooxon were detected. Irradiation of hydroxymethylfenitrothion in oxygenated hexane produced formylfenitrothion, carbomethoxyfenitrothion, and carbomethoxynitrosofenitrothion (Greenhalgh and Marshall, 1976).

FENSULFOTHION (Dasanit, Bayer 25141) [O,O-Diethyl O-(p-methylsulfinylphenyl)phosphorothioate]

When cell suspension of Klebsiella pneumoniae were incubated with fensulfothion, a metabolite formed. Combined GC-MS and IR were used to identify this compound as fensulfothion sulfide (Wood and Mac Rae, 1977).

Carrots grown in muck soil contained measurable amounts of the sulfone in all sections of the carrot (Finlayson et al., 1976). When grown in soil treated the previous year at 5.6 kg a.i./ha, carrots exhibited a residue of about 0.10 ppm (Chisholm, 1974).

Laboratory studies were conducted to assess fensulfothion persistence in soil. Persistence varied from 50-60 days with concentrations of 50-175 ppm. At concentrations of 250 ppm or more, fensulfothion persisted for more than 900 days in soil (Sheela and Vasantharajan, 1977).

A number of soil bacteria, Nocardia spp. and Arthrobacter spp., degraded the products of fensulfothion hydrolysis and oxidation: 4-methylmercaptophenol (MMP); 4-methylsulfinylphenol (MSP); and 4-methylsulfonylphenol (MSO_2P). Nocardia calcarea hydroxylated the ring to form a substituted catechol. Meta cleavage between carbons 2 and 3 ensued to give 2-hydroxy-5-methylmercaptomuconic semialdehyde from MMP and the corresponding sulfinyl analog from MSP. MSO_2P was hydroxylated to form 4-methylsulfonylcatechol. In this case, ortho cleavage occurred, splitting the ring between atoms 1 and 2 to form 3-methylsulfonylmuconic acid (Rast et al., 1978).

FENTHION [*O*,*O*-Dimethyl *O*-(4-methylthio)-*m*-tolyl phosphorothioate]

In parathion resistant houseflies, fenthion oxidation and sulfoxidation were greater than in fenthion resistant flies. This resulted in greater production of the more toxic metabolites fenoxon and fenthion sulfoxide (MacDonald, 1976).

FLUENETHYL (Flu) [2-Fluorethyl 4-biphenylylacetate]

Human, mouse, sheep, and pig plasma degraded Flu. Biphenylylacetic acid was the major product. Mice were administered Flu intraperitoneally. Analysis of urine indicated the presence of biphenylylacetic acid, 2-hydroxybiphenyl, 4-hydroxybiphenyl, 4,4'-dihydroxybiphenyl, biphenyl, and 3,4-dihydroxybiphenyl. Subcellular hepatic preparations also produced biphenylylacetic acid and the hydroxy metabolites. In the urine analyzed, biphenylylacetic acid and the hydroxybiphenyls occurred free and conjugated as glucuronides and/or sulfates (Johannsen, 1974).

In vivo and *in vitro* metabolism of Flu by houseflies and twospotted spider mites was qualitatively alike and the metabolites were the same as the free compounds observed in mouse urine except 2-hydroxybiphenyl, which was not observed in spider mites (Johannsen, 1974).

When mice, houseflies and spider mites were exposed to fluenethyl, high levels of citrate were accumulated, indicating monofluoroacetate conversion to fluorocitrate and blocking of the enzyme aconitase. These studies showed that ester hydrolysis, *in vitro* and *in vivo*, occurred with formation of monofluorethanol, which was subsequently metabolized to the monofluoracetate, and 4-biphenylacetate. In addition to these compounds, 2-hydroxy-, 4-hydroxy-, 4,4'-dihydroxy- and 3,4-dihydroxy- biphenyl, conjugates of the hydroxy metabolites, and biphenyl were also present (Johannsen and Knowles, 1974; Knowles, 1974 and 1976).

FLUOROACETATE

Preparations of rat livers exhibited an ability to defluorinate fluoroacetate. Greatest activity resided in the 105,000g supernatant. Glutathione significantly increased defluorination (Kostyniak et al., 1978).

In Gloeocapsa sp., a unicellular blue-green nitrogen-fixing alga, fluoroacetate metabolism resulted in formation of fluorocitrate (Gallon et al., 1978).

FLUORODIFEN [2,4'-Dinitro-4-trifluoromethyl diphenyl ether]

Rats were treated with ^{14}C-fluorodifen. Analyses of urine showed that about 83% of the radioactivity present in the urine was accounted for by one metabolite identified by MS as 2-nitro-4-trifluoromethylphenyl mercapturic acid (Lamoureux and Davison, 1975).

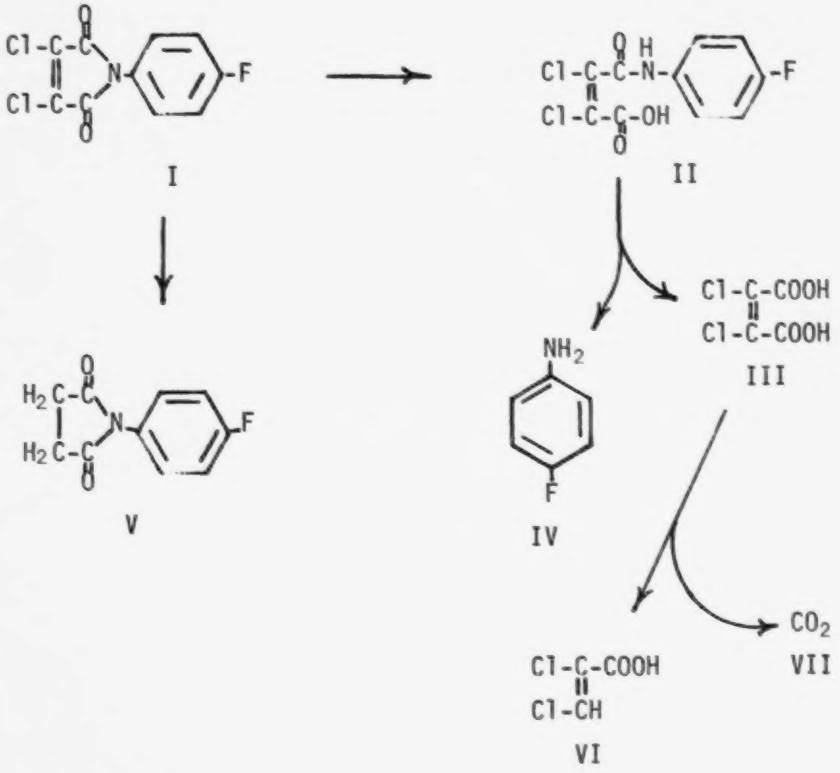
In petiole-excised peanut leaves, fluorodifen ether bond was cleaved. Two major metabolites and a minor one, 2-nitro-4-trifluoromethylphenol, were formed. The 4-nitrophenol metabolite formed two water soluble conjugates. The 2-nitro-4-trifluoromethylphenyl moiety formed the glutathione conjugate. The glutathione S-transferase involved was isolated from peanut hypocotyls, corn seedling shoots, and squash hypocotyls. This was specific for GSH and catalyzed cleavage of fluorodifen to give equimolar amounts of GS-conjugate and 4-nitrophenol (Shimabukuro et al., 1973). In addition to the GS-conjugate of 2-nitro-4-trifluoromethylphenol, *p*-nitrophenyl-6-*O*-malonyl-β-D-glucoside, *p*-nitrophenyl-β-D-glucoside, and *S*-(2-nitro-4-trifluoromethylphenyl)-*N*-malonylcysteine were also observed (Shimabukuro et al., 1976). The GSH-S-transferase catalyzes formation of a fluorodifen-GSH conjugate which does not appear to be metabolized to mercapturic acids in plants (Shimabukuro et al., 1977).

When fluorodifen was added to a culture of soil microorganisms, nitrite was produced at concentrations up to 80% of the fluorodifen nitro-nitrogen present. 4-Nitrophenol and quinol were also observed (Tewfik and Hamdi, 1975).

Six months after application of fluorodifen to soil, less than 10% remained (Walter et al., 1970).

FLUOROIMIDE (Spartcide) [2,3-Dichloro-N-(4-fluorophenyl)maleimide]

When applied to apple trees, fluoroimide was degraded to compounds II, III, IV, and V. In soil, in addition to these compounds, fluoroimide was converted into compound VI and CO_2 (VII). Compounds II and CO_2 were the major products in soil. Metabolite II was observed more under a flooded condition than in an upland condition. On the other hand, CO_2 was more rapidly generated under aerobic than anaerobic conditions. The fluoroimide $t_{1/2}$ in soil was less than one day (Ogawa et al., 1978).



FLURIDONE [1-Methyl-3-phenyl-5-(3-trifluoromethylphenyl-4(1H)-pyridinone]

Fluridone was applied to cotton (Gossypium hirsutim L. 'Stoneville 213'), corn (Zea mays L. 'Migro 5040'), soybean (Glycine max L. Merr. 'Calland'), and rice (Oryza sativa L. 'Nato'). Metabolism studies indicated that tolerance resulted from limited translocation of absorbed fluridone (Berard et al., 1978).

When added to ponds, the fluridone $t_{1/2}$ in the water column was 4 to 7 days; in the hydrosoil, the $t_{1/2}$ was greater than 3 months (Muir and Grift, 1978).

FMC 25213 (*r*-2-Ethyl-5-methyl-*c*-5-(2-methylbenzyloxy)-1,3-dioxane]

Under acidic conditions FMC 25213 breaks down to propionaldehyde and 2-methylbenzyl 1,3-dihydroxy-2-methylprop-2-yl ether (Selim and Cook, 1978).

FOLPET [N-Trichloromethylthiophthalimide]

The glutathione-dependent methyltransferase enzyme system was inhibited by folpet. Phthalimide was the main product formed from folpet. There were indications that 2-thiazolidinethiones were also formed (Davidek and Seifert, 1975).

When folpet was reacted with thiamine-thiol, a compound was observed that released thiamine and exhibited an IR spectrum similar to the product obtained from the reaction of thiophosgene with thiamine (Seifert and Davidek, 1977).

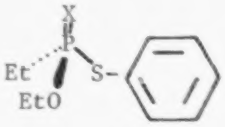
The reaction of folpet with GSH produced GSSG as the primary product. About five unidentified products were also formed. These compounds contained all or a portion of the $-SCCl_3$ moiety. Gaseous materials released included COS (Siegel, 1970).

FONOFOS (Dyfonate) [O-Ethyl S-phenyl ethylphosphonodithioate]

When labeled fonofos was incubated with mouse liver mixed-function oxidase, stereoselective metabolism occurred with $(S)_P$-fonofos giving predominantly the $(R)_P$-oxon and $(R)_P$-fonofos giving the $(S)_P$-oxon. Some racemization also occurred. Diphenyl disulfide (DPDS) and diphenyl disulfide oxide were also observed. In the presence of mouse and rat serum, fonofos was stable; however, the oxon slowly gave rise to DPDS (Lee, 1977; Lee et al., 1978a).

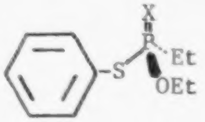
When phenyl-^{35}S-fonofos was administered to mice, the $(S)_P$-isomer was eliminated, primarily in urine, more rapidly than the $(R)_P$-isomer. In addition to unchanged fonofos, other identified ^{35}S-labeled metabolites included: fonofos oxon, diphenyl disulfide, diphenyl disulfide oxide, methyl phenyl sulfoxide and sulfone, and 3-OH- and 4-OH-phenyl methyl sulfones. When phenyl-^{35}S-fonofos oxon was used, ^{35}S-labeled metabolites included methyl phenyl sulfoxide, methyl phenyl sulfone, and 3-OH- and 4-OH-phenyl methyl sulfones (Lee et al., 1978b).

After topical application of phenyl-^{35}S-fonofos to houseflies, unchanged fonofos was the main compound in the external wash. In addition some oxon, methyl phenyl sulfoxide, and methyl phenyl sulfone were also observed. Internally, in addition to unchanged fonofos, metabolites identified included diphenyl disulfide, methyl phenyl sulfoxide and sulfone, and 3-OH- and 4-OH-phenyl methyl sulfones (Lee et al., 1978c).



X=S $(S)_P$

X=O $(R)_P$



X=S $(R)_P$

X=O $(S)_P$

^{14}C-Ring- and ^{14}C-ethoxy-labeled fonofos was incubated with the soil fungus *Rhizopus japonicus*. Four metabolites were identified by GLC and MS: fonofos oxon; O-ethyl ethylphosphonic acid; thiophenol; and methyl phenylsulfone. Other compounds were found in the mixture but their origin was not clear: O-ethyl S-phenyl methylphosphonodithioate and its oxon analog; O-ethyl S-phenyl butylphosphonodithioate; and bis(phenylsulfide) (Lichtenstein et al., 1977a).

Under Quebec, Canada, weather conditions (May-August), somewhat more than half of the fonofos applied to soil disappeared in about 4 months

(Khan et al., 1976b). In other studies under subtropical conditions, only 36% of fonofos applied to soil was recovered after 6 weeks. The rate of degradation increased with subsequent applications (Talekar et al., 1977b).

In pea plants, dyfonate was converted in part to its oxon analog (Talekar, 1974).

Soil fungi degraded dyfonate primarily to dyfoxon, *O*-ethyl ethylphosphonothioic acid, *O*-ethyl ethylphosphonic acid, methyl phenyl sulfoxide, and methyl phenyl sulfone. In soil, the fungus *R. arrhizus* metabolized dyfonate to the oxon and water-soluble unidentified metabclites (Flashinski, 1974).

The adsorption of dyfonate on humic acid, saturated with various cations, was studied. Adsorption was affected by the cation. Data suggested physical adsorption and the Freundlich constants, K and $\frac{1}{n}$, decreased and increased, respectively, with increase in temperature (Khan, 1977).

FORMOTHION (Anthion) [O,O-Dimethyl S-(N-methyl N-formylcarbamoylmethyl) phosphorodithioate]

Enzyme preparations were made from livers of white male Dublin Sprague-Dawley rats. These preparations were incubated with ^{14}C-formothion. After extraction of the mixture, TLC was used to separate the products. All formothion was altered within 30 minutes. The only metabolites identified were dimethoate and dimethoate monoacid. Similar results were obtained with denatured enzyme preparations. Additional studies indicated that the breakdown of formothion was dependent primarily on pH of the solution (El-Oshar and Dauterman, 1977).

See also Dimethoate.

FRESCON [N-Tritylmorpholine]

Fish (S. mossambicus) were exposed to frescon for 22 h. Analyses of fish indicated the presence of unchanged frescon and a small amount of morpholine. Similar results were observed when bile was analyzed (Matthiessen, 1977).

FTHALIDE [4,5,6,7-Tetrachlorophthalide)

When added to a laboratory prepared compost, fthalide (I) readily degraded to water soluble compounds. In benzene and ethyl acetate extracts of compost treated with ^{14}C-labeled fthalide, 18 degradation products were identified:

II. 4,5,6-trichloropnthalide
III. 4,6,7-trichlorophthalide
IV. 4,6-dichlorophthalide
V. 4,7-dichlorophthalide
VI. 4-chlorophthalide
VII. 4,5,6-trichloro-7-methylthiophthalide
VIII. 4,6,7-trichloro-5-methylthiophthalide
IX. 3,4,5,6-tetrachlorophthalic acid
X. 3,4,5-trichlorophthalic acid
XI. 3,4,6-trichlorophthalic acid
XII. 3,5-dichlorophthalic acid
XIII. 3,6-dichlorophthalic acid
XIV. 4,5-dichlorophthalic acid
XV. 4-chlorophthalic acid
XVI. 3,5-dichloro-4-methylthiophthalic acid
XVII. 4,5-dichloro-3-methylthiophthalic acid
XVIII. 4-chloro-5-methylthiophthalic acid
XIX. 3,4,5,6-tetrachloro-2-hydroxymethylbenzoate.

(Tokuda et al., 1976)

GLYPHOSATE (Glyphosine) [N-(Phosphonomethyl)glycine]

When applied to leaves, glyphosate moved to other leaves, buds and developing fruit on the same branch. Analyses indicated the presence of one metabolite in addition to unchanged glyphosate. The metabolite was identified as aminomethylphosphonic acid (Putnam, 1976).

One week after application of glyphosate to Canada thistle (*Cirsium arvense* L.) and leafy spurge (*Euphorbia esula* L.) analyses did not reveal the presence of metabolites (Gottrup et al., 1976).

Field bindweed, Canada thistle, and tall morningglory were treated with ^{14}C-glyphosate. Each of the test species contained traces of aminomethylphosphonic acid (AMP) and sarcosine (Sandberg, 1978; Sandberg et al., 1978).

Studies of glyphosate metabolism in soil indicated initial rapid inactivation by adsorption. The studies also indicated that glyphosate does not sustain microbial growth and that degradation was by co-metabolism (Torstensson and Aamisepp, 1977). When ^{14}C-labeled glyphosate was incubated with sterilized soils, the formation of $^{14}CO_2$ was negligible, indicating that chemical degradation was not a major pathway. In the presence of soil microflora, degradation was rapid with formation of $^{14}CO_2$. The main soil metabolite was identified as aminomethylphosphonic acid. Other metabolites identified included: N-methylaminomethylphosphonic acid; glycine; N,N-dimethylaminomethyl-phosphonic acid; and hydroxymethylphosphonic acid. Several other metabolites were not identified. Two compounds were identified as conjugates of glyphosate and aminomethylphosphonic acid. Exposure to UV indicated that photodecomposition was minimal. Characterization of soil metabolites was done with the aid of NMR and MS methods (Rueppel et al., 1977). In five Hawaiian sugarcane soils, glyphosate degradation was dependent on soil binding, pH, and organic matter. $^{14}CO_2$ evolution was constant after 16-21 days. After 60 days, the residues consisted of glyphosate and aminomethylphosphonic acid (Nomura and Hilton, 1977). Glyphosate complexed strongly with clay containing Al, Fe, Zn or Mn but did not bind with clay complexed with Mg, Ca, or Na. Muck soil and charcoal bound glyphosate but ethyl cellulose did not (Sprankle et al., 1973).

In soil treated with nitrite and glyphosate, formation of N-nitrosoglyphosate was observed. This was not pH dependent in the range 3.6-6.1 (Khan and Young, 1977).

The major glyphosate metabolites in sugarcane were identified as amino-bis-methylenephosphonic acid, N-methylamino-bis-methylenephosphonic acid, N-phosphonomethylglycine, and N-methyl-N-phosphonomethylglycine (Marvel et al., 1975).

Glyphosate degraded rapidly in soil. In short-term laboratory studies, the formation in soil of aminoethylphosphonic acid (AMP) in free and bound forms and glyphosate in bound form was observed. NMR and MS were used to characterize the metabolites. In hydroponic studies with corn, cotton, soybeans and wheat, glyphosate was converted to AMP and glyoxylate. This was then incorporated into natural products. In soybeans hydroponically treated with glyphosate, AMP was also seen (Rueppel and Marvel, 1975; Rueppel et al., 1975a, b and c).

In soil, ^{14}C-glyphosate underwent micrcbial degradation with release of $^{14}CO_2$. Reduced glyphosate degradation occurred when Fe^{+++} and Al^{+++} were added. This probably was caused by adsorption on colloidal Fe and Al precipitates (Moshier and Penner, 1978). Mineral soils significantly reduced inhibitory effects of glyphosate on root growth (Hensley et al., 1978).

Glyphosate was applied to empty irrigation canals. Soil samples taken 23 weeks after application contained glyphosate and aminomethylphosphonic acid. When water was allowed to flow in the canals, glyphosate disappearance was not rapid and 58% of the dose was present 8 to 14.4 km downstream (Comes et al., 1976).

GUAZATINE (1,17-Diguanidino-9-azaheptadecane) [Bis(8-guanidinooctyl) amine]

Under alkaline conditions, guazatine underwent hydrolysis to bis(8-aminooctyl)amine. This was confirmed by MS and IR (Lynch, 1974).

HCB [Hexachlorobenzene]

HCB was administered in the diet to female rhesus monkeys at the rate of 1 ppm for 550 days. A graph of storage indicated that a leveling of curve began after 300 days and, when extrapolated, plateaus at 700 to 750 days. After 450 days, about 0.5% was excreted as PCB and only traces of PCP. Long-term studies conducted with Rhesus monkeys exposed to HCB indicated that long-term storage in fat occurred with only about 30% of the administered dose excreted in urine and feces after one year. Metabolism also was slow with only 4.4% of the dose excreted as metabolites after one year. The major metabolite was identified as pentachlorophenol (PCP). Traces of pentachlorobenzene (PCB) were also observed. Other metabolites were observed but not identified (Yang et al., 1978).

When ^{14}C-HCB was administered i.v. to male rats, little or no radioactivity was exhaled (Yang and Pittmen, 1975). Female rats absorbed ^{14}C-HCB in oil. About 70-80% of the label was excreted in feces as unchanged HCB. The rest of the activity, consisting of metabolized HCB, contained PCP and tetrachlorohydroquinone (Koss and Koransky, 1975). In rats the primary metabolite of HCB was PCP (Lui and Sweeney, 1975). In other studies with rats given HCB, PCP was found in urine and feces, 2,3,5,6-TeCP in feces, and 2,4,5-TCP in urine, PCB in urine and feces, 1,2,3,4-TeCB in urine, 1,2,4,5-TeCB and 1,3,5-TCB in urine (Renner et al., 1978b).

Wistar rats were administered HCB by gavage. Analysis of organs showed the presence of HCB, Pentachlorophenol (PCP), and pentachlorobenzene (PCB). Feces contained large amounts of HCB and some PCB. Urine, however, contained PCP, PCB, 2,4,6-TCP, and TeCP (2,3,4,6- and/or 2,3,5,6-tetrachlorophenol) in the free form and 2,4,6-TCP and 2,3,4,6-TeCP as glucuronide conjugates (Engst et al., 1976a). After intraperitoneal dosing of female rats with HCB, urine and feces were collected. GC and GC-MS were used to identify the metabolites: PCP, tetrachlorohydroquinone (TeCH), pentachlorothiophenol (PCThP), and tetrachlorothiophenol (TeCThP) (Koss et al., 1976). Elimination of HCB from female rats exhibited a $t_{1/2}$ = 4-5 months. After 9 weeks' exposure to HCB, there was an equilibrium between intake and excretion of HCB and metabolites. Analysis of liver showed the presence of PCP, TeCH, and PCThP (Koss et al., 1978). In other studies, analysis of rat urine showed the presence of N-acetyl-S-(pentachlorophenyl)cysteine (PCC). TLC, HPTLC, UV, IR and MS were used to identify this metabolite. Some free PCP was also observed (Renner et al., 1978a).

HCB in peanut oil was administered to Wistar rats. Urine and feces analyses showed the presence of tetrachlorothiophenol, pentachlorothiophenol, methylthiopentachlorobenzene, methylthiotetrachlorobenzene, tetrachlorobenzenedithiol and/or its monomethylthio-analog, and 1,4-bis(methylthio)-2,3,5,6-tetrachlorobenzene (Jansson and Bergman, 1978). 2,4,5-TCP was also isolated from urine of rats (Renner and Schuster, 1977). Whole body half-life was calculated as 60 days (Morita and Oishi, 1975).

Laying pullets were administered oral doses of HCB. More than half the residue was excreted in egg yolks. The $t_{1/2}$=24-27 days (Hansen et al., 1978).

When fed to green sunfish (*Lepomis cyanellus* Raf.), HCB gave rise to PCP. The $t_{1/2}$=14-28 days (Sanborn et al., 1977a).

HCB volatilized rapidly from plant and soil surfaces but seemed to persist in soil (Beall, 1976). Bioaccumulation ratios were calculated:

Species	Factor
Algae (*Oedogonium cardiacum*)	570
Snail (*Helisoma* sp.)	75
Daphnids (*Daphnia magna*)	120

(Isensee et al., 1976)

In a model ecosystem, HCB was degraded to polar metabolites and conjugates. Pentachlorophenol (PCP) was present in the water phase in appreciable amounts. HCl hydrolysis of polar products found in the water gave a family of chlorinated phenols (Metcalf et al., 1973b). It has been reported that in rats 2,4,5-trichlorophenol was produced in addition to PCP (Mehendale, unpubl., in Metcalf et al., 1973).

When HCB was exposed to sunlight on silica gel or as a crystalline material, photodecomposition was slow. When conducted in methanol or hexane at $\lambda>260$ or 220 nm, photolysis was rapid and the expected PCB and TeCB were obtained. The reaction of HCB with methanol also produced pentachlorobenzyl alcohol and traces of a compound believed to be tetrachlorodi(hydroxymethyl)benzene (Plimmer and Klingebiel, 1976).

Destruction of HCB by combustion is difficult at 800 C. Temperatures of at least 950 C are required if residues were to be less than 100 mg HCB/Kg HCB burned (Ahling and Lindskog, 1978).

HEXACHLOROPHENE (HCP) [2,2'-Methylene bis(3,4,6-trichlorophenol]

Rats given HCP intraperitoneally excreted about 5% of the dose in urine and none as CO_2. More than 70% of the material was excreted in feces. Whereas urine contained HCP only as a conjugate, probably the glucuronide, feces contained HCP both free and conjugated (Black et al., 1974).

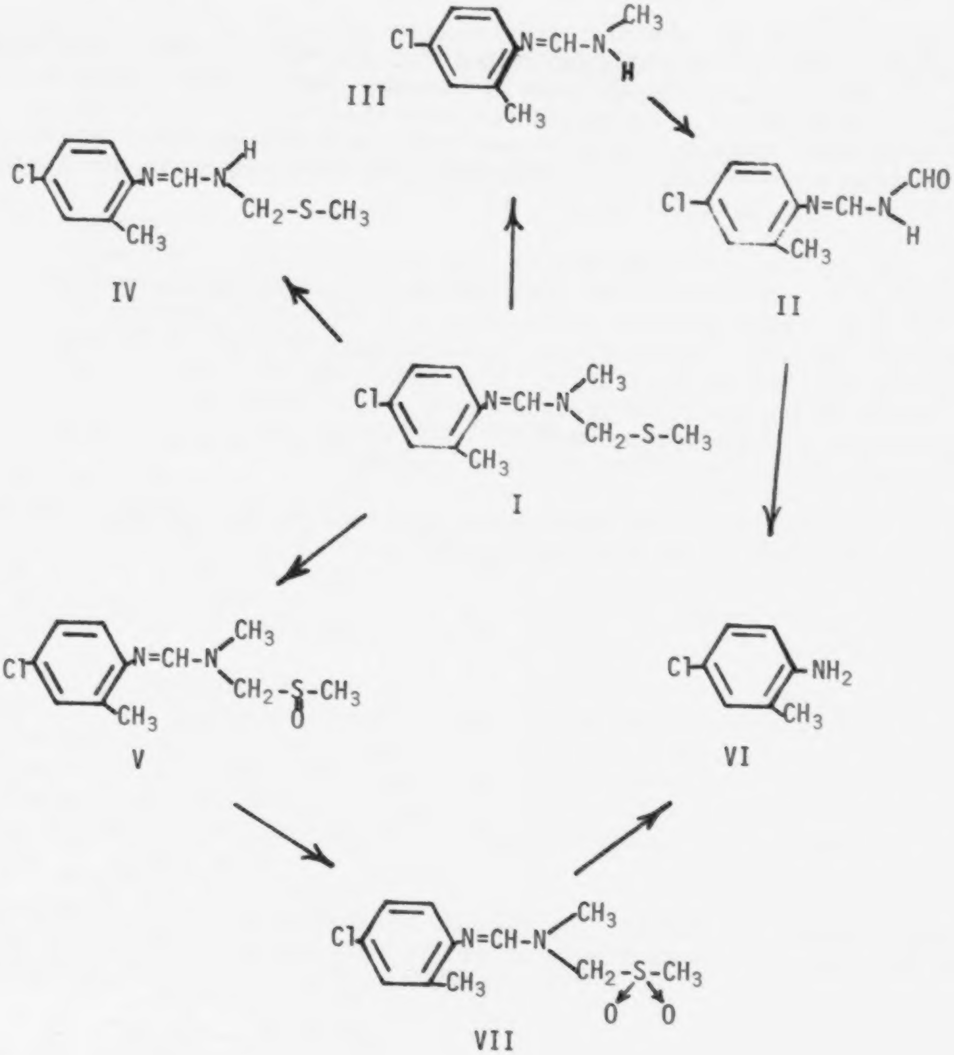
Hexachlorophene was administered intraperitoneally to rats and rabbits. Excretion of this chemical was slow, most (48-83%) excreted unchanged in the feces. Both rat and rabbit formed a glucuronide conjugate of hexachlorophene which accounted for more than half of the urinary metabolites. A monoglucuronide conjugate was also excreted in the bile (Edelson and McMullen, 1976; Gandolfi, 1973; Gandolfi and Buhler, 1974 and 1977; Gandolfi et al., 1972).

HCP was applied to peanut plants. No translocation of HCP was detected and no evidence of plant metabolism of HCP was detected. Since all compounds observed on treated plants were observed on controls as well, the evidence indicated that UV photolysis was responsible for HCP alteration. Two compounds observed, in addition to about 12 unidenified products were: 2,2'-dihydroxy-3,5',6,6'-tetrachlorodiphenylmethane and 2,2'-dihydroxy-3,5,5',6,6'-pentachlorodiphenylmethane (Van Auken and Hulse, 1978).

Other studies have shown that hexachlorophene forms hydrogen bonding to polypeptides (Haque and Buhler, 1972).

HOKUPANON (Hokko-20013) [*N*-(4-Chloro-*o*-tolyl) *N*-methylthiomethyl *N* -methylformamidine]

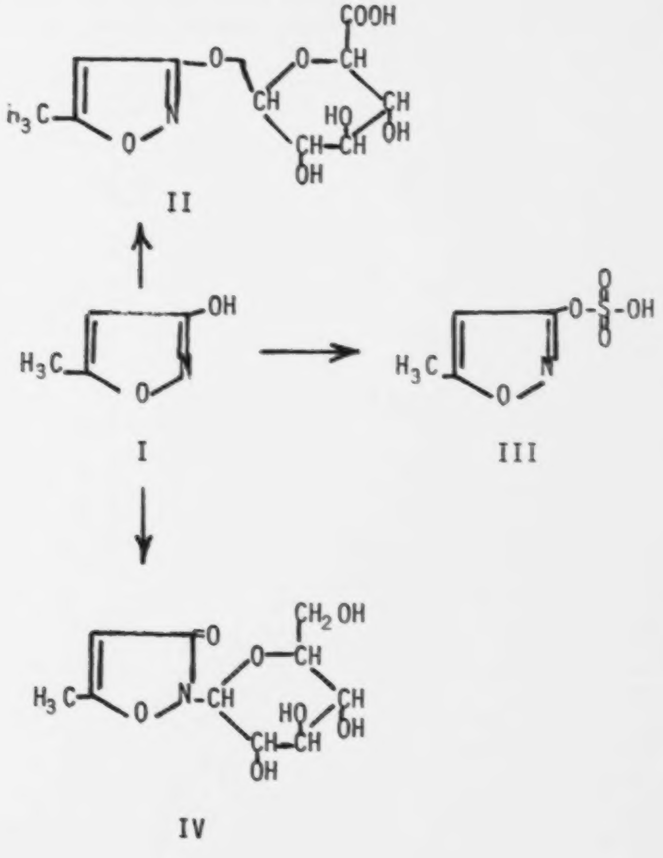
The metabolism of Hokupanon in rice is summarized in the following diagram (Knowles, 1976).



HYMEXAZOL [3-Hydroxy-5-methylisoxazole]

Labeled hymexazol was administered in single oral doses to Wistar rats. Absorption was rapid and 97% of the dose was excreted in urine within 96 h. NMR and IR were used to identify two metabolites found in the urine as 3-(β-D-glucopyranuronosyloxy)-5-methylisoxazole (II) and 5-methyl-3-isoxazolyl sulfate (III). A small amount of labeled CO_2 was also observed (Ando et al., 1974).

Hymexazol was applied to cucumber, tomato, and rice plants. Absorption into roots and translocation into leaves was rapid. Two metabolites were isolated from plant tissues and identified as the glucose conjugate (II) and 2-(β-D-glucopyranosyl)-5-methyl-4-isoxazolin-3-one (IV). Some $^{14}CO_2$ was also formed from labeled hymexazol (Kamimura et al., 1974).



IMUGAN [N-Formyl-N'-(3,4-dichlorophenyl)-2,2,2-trichloroacetaldehydeaminal]

Excretion of ^{14}C-imugan administered to rats was rapid. By the 20th day, rats were excreting 95% of the daily dose (Viswanathan et al., 1976). The initial product of degradation was identified by MS as 3,4-dichloroaniline. Other metabolites found in urine and feces included: 3,4-dichloroaminophenol; 6-hydroxy- and 6-methoxy- 3,4-dichloroacetanilide; 3,4-dichloroacetanilide; 3,4-dichloroformanilide; 3,4-dichlorophenylisocyanate; 6-methoxy-3,4-dichloroaniline; and methyl N-(3,4-dichlorophenyl)carbamate. Three other compounds were observed but not identified (Viswanathan et al., 1978a).

Imugan was applied to soil. Subsequently, soil residues were shown to contain 3,4-dichloroaniline and 3,3',4,4'-tetrachloroazobenzene (TCAB) (Sotiriou et al., 1976).

Algae, exposed to imugan, have been found to form a ring hydroxylated analog of 3,3',4,4'-TCAB (Moza, unpublished, in Viswanathan et al., 1976).

INEZIN [*S*-Benzyl *O*-ethyl phenylphosphonothiolate]

Inezin in *n*-hexane was exposed to UV irradiation. Initial cleavage of the P-S bond produced *O*-ethyl phenylphosphinate and dibenzyl disulfide. Degradation of the latter gave toluene-α-sulfonic acid which in turn gave benzoic acid and sulfate. Other products were identified as *O*-benzyl *O*-ethyl phenylphosphonothionate and its oxygen analog, phenylphosponic acid, *O*-ethyl hydrogen phenylphosphonothioate and its oxygen analog, and benzyl alcohol (Murai and Tomizawa, 1976; Murai, 1978).

IODOFENPHOS (Ciba C-9491) [O-(2,5-Dichloro-4-iodophenyl) O,O-dimethyl phosphorothioate]

Studies, preliminary to development of analytical methodology for iodofenphos metabolites, indicated that iodofenphos in hexane underwent photolytic degradation when exposed to sunlight or fluorescent light. The oxon behaved similarly. No products were identified. In CCl_4, exposure to sunlight produced a compound with the retention time of ronnel and the color of molecular iodine in the CCl_4. Treatment of an Angora goat with iodofenphos produced some 4-iodophenol in the urine only (Ivey and Oehler, 1976).

ISOFENPHOS (BAY 92114) [*O*-Ethyl *O*-2-isopropoxycarbonylphenyl isopropylphosphoramidothioate]

In studies with field-treated potatoes, residues consisted of isofenphos and its oxygen analog (Brown and Williams, 1976).

ISOTHIAZOLONES

5-Chloro-2-methyl-4-isothiazolin-3-one calcium chloride (I)
2-Methyl-4-isothiazolin-3-one calcium chloride (II)

The environmental fate of compounds I and II was studied. Hydrolysis increased with increasing pH and temperature. Both compounds were degraded by UV. Degradation occurred in rats, fish, ferns and sludge. Not all compounds were observed in all systems, but a common denominator linked all. Products identified or indicated by these studies included loss of chloride and sulfur, N-methylmalonic acid, malonamic acid, malonic acid, acetic acid, formic acid, CO_2, 5-chloro-2-methyl-4-isothiazolin-1-oxide, N-methylglyoxylamide, ethylene glycol and urea (Krzeminski et al., 1975a and b).

ISOXATHION (Karphos) [*O*,*O*-Diethyl *O*-(5-phenyl-3-isoxazolyl)phosphorothioate]

Bean, cabbage and Chinese cabbage plants were exposed to ^{14}C-isoxathion. After penetration into the plants, isoxathion was rapidly hydrolyzed to give 3-hydroxy-5-phenylisoxazole. This was conjugated with glucuronic acid. A derivative of this conjugate was observed but not further identified. Oxidation of the 3-hydroxy-5-phenylisoxazole produced the corresponding ketone which was found as the *N*-glucuronides of 5-phenyl-4-isoxazolin-3-one and 5-(4-hydroxyphenyl)-4-isoxazolin-3-one. Cleavage of the isoxazole ring to benzoylacetamide occurred with subsequent formation of benzoic acid (Ando et al., 1975). The half-life of isoxathion in or on kidney beans was 5 days (Nakamura et al., 1977).

Juvenile Hormones (JH)

ALTOSID

ECDYSONE

GOSSYPLURE

GRANDLURE

HYDROPRENE

JH-I

METHYL FARNESOATE

PRECOCENE II

R-20458

RO-10-3108

RO-20-3600

In *M. sexta* larvae, a binding protein acts as a carrier for the JH. This prevents hydrolyses by general esterases present in the tissues and protects the JH. The JH-esterases are specific and distinct from the general esterases present in the haemolymph of *M. sexta* larvae. The specific enzyme was found in the fat body and target tissues (Sanburg et al., 1975).

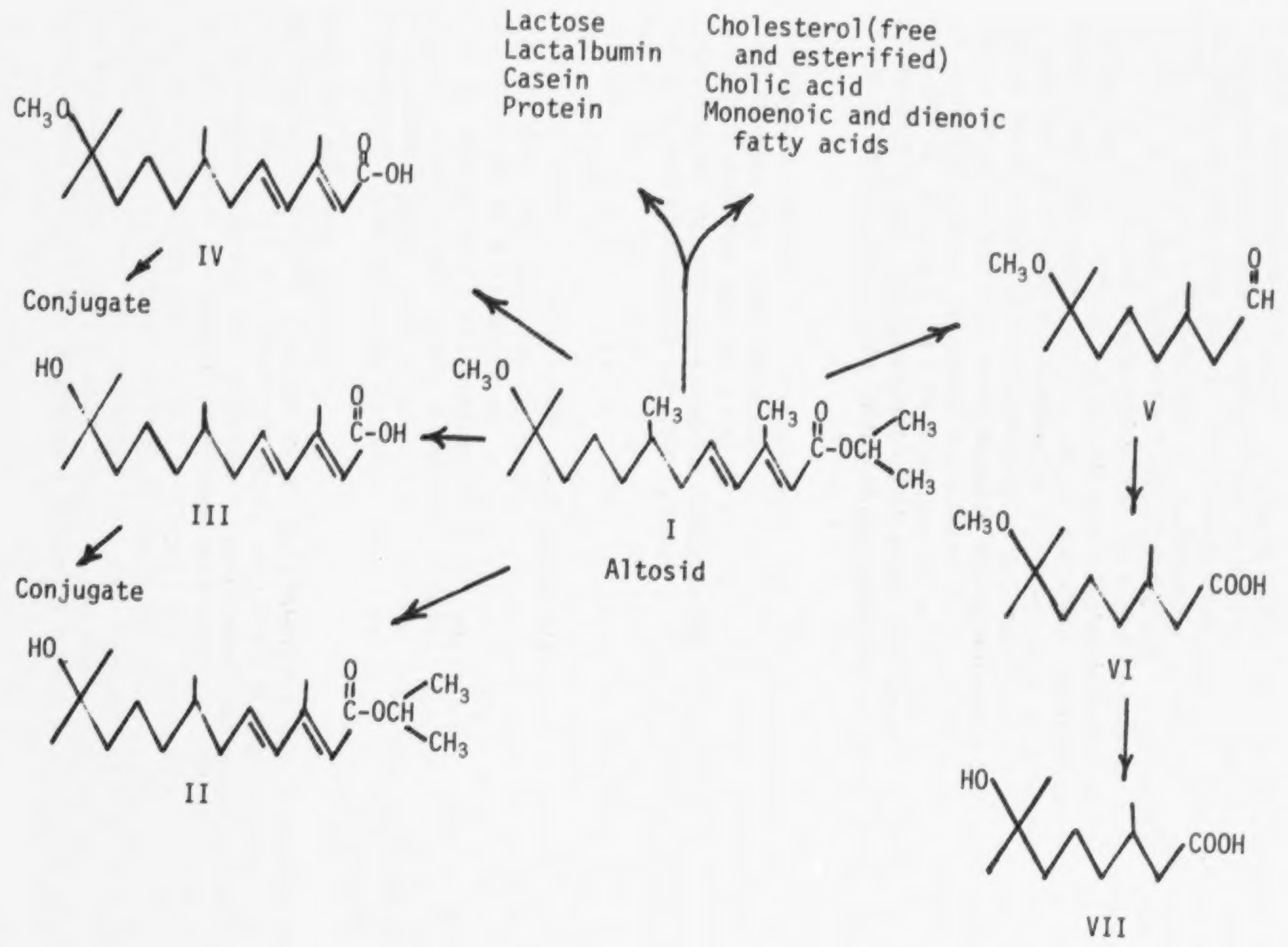
The binding of juvenile hormones to proteins was investigated with JH-1, methoprene and Bowers' 2b. These compounds exhibited binding constants of 10^5 to 10^6 M^{-1} with indications that the binding was electrostatic in nature. With oxidized cytochrome P_{450}, Type I complexes formed (Mayer and Burke, 1976).

ALTOSID (Methoprene, ZR 515) [Isopropyl 11-methoxy-3,7,11-trimethyldodeca-2,4-dienoate]

When ^{14}C-methoprene was administered orally to rats, slightly less than 20% was excreted within 5 days in the urine and a similar amount in feces and almost 40% was excreted as $^{14}CO_2$. About 17% was retained in the body. Highest concentrations were in liver (84.5 ppm), kidneys (29 ppm), lungs (26 ppm), fat (36.5 ppm), and the adrenal cortex (12-13 ppm). About 12 labeled compounds were detected in the urine but no unchanged methoprene was observed. The metabolites were not identified but the available evidence indicated that they probably arose via β-oxidation. Expected products of ester hydrolysis and O-demethylation were not detected (Hawkins et al., 1977).

A Hereford steer received a single oral dose of [5-^{14}C]methoprene and sacrificed 2 weeks later. No primary metabolites were observed in fat, muscle, liver, lung, blood and bile. However, the majority of the tissue radioactivity was present as [^{14}C]cholesterol. About 72% of the activity in bile appeared in cholesterol, cholic acid, and deoxycholic acid. Protein and cholesteryl esters of fatty acids also contained some radioactivity. When administered to a lactating cow, [5-^{14}C]methoprene gave rise to randomly labeled acetate. This was incorporated into milk fat which was degraded to saturated and mono- and di- enoic fatty acids. Labeled lactose, lactalbumin, casein, and free and esterified cholesterol was also observed (Quistad et al., 1975a and c; 1976c). Analyses of steer urine showed the presence of compounds II, III, IV and V, free and conjugated. Similar qualitative results were observed in urine of a guinea pig orally dosed with methoprene. Quantitative differences were observed (Chamberlain et al., 1975).

About 4 mg ^{14}C-methoprene was administered orally to colostomized chickens. $^{14}CO_2$ was the main ^{14}C-product detected. When large doses were given, elimination was greatest in urine and ^{14}C was also found in the eggs and all tissues and organs examined (Davison, 1976). In addition to natural ^{14}C-cholesterol and ^{14}C-fatty acid triglycerides, there were metabolites conjugated to glycerol and/or cholesterol. Urine contained uric acid and compounds III and IV as conjugates. Feces contained compounds II, III and IV and each had undergone considerable isomerization. About 19% of the ^{14}C appeared in the eggs. Most of this was associated with egg proteins. The egg yolks also had radiolabeled fatty acid glycerides and cholesterol. The metabolite glycerides were di- and tri- glycerides of compounds VIII and IX. Two other primary metabolites in egg yolks were compounds III and IV. Blood contained radiolabeled cholesterol and traces of cholesteryl esters. Tissue residues were similar to those found in eggs (Quistad et al., 1976b).

Lactose
Lactalbumin
Casein
Protein
Cholesterol(free and esterified)
Cholic acid
Monoenoic and dienoic fatty acids
CH3O
C-OH
IV
Conjugate
HO
III
CH3
C-OCH
I
Altosid
Conjugate
II
CH
V
COOH
VI
VII

In a dynamic flow-through system, bluegill sunfish (Lepomis macrochirus) concentrated unchanged methoprene to levels about 300 times above the exposure level. When transferred to untreated flowing water, the fish eliminated more than 90% of the residues within 2 weeks. In a model ecosystem, the labeled methoprene was metabolized and ^{14}C was incorporated into cholesterol, free fatty acids, natural glycerides and protein. Small amounts of compound II was also observed in the fish 2 weeks after treatment (Quistad et al., 1976a).

Larval mosquitoes and houseflies were exposed to methoprene. In the third- and fourth-instar Aedes and fourth-instar Culex larvae, the hydroxy ester was the predominant primary metabolite; in the third-instar Culex larvae, the hydroxy acid predominated. Other metabolites observed were:

Mosquito larvae

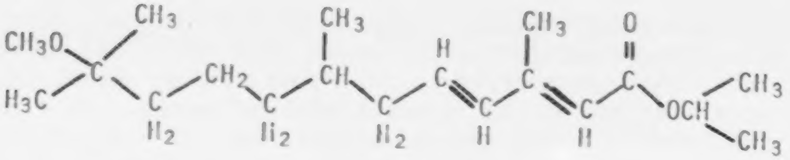
Hydroxy ester (II) (free and conjugated)
Hydroxy acid (III) (free and conjugated)
Methoxy acid (IV)
Metabolite (VI)
Metabolite (VII) (free and conjugated)

Housefly larvae

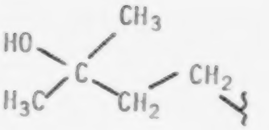
Hydroxy ester (II)
Hydroxy acid (III) (free and conjugated)
Metabolite (V)
Metabolite (VI)
CO_2

This study also showed that isomerization was an effective detoxication mechanism and that insects can rapidly isomerize the 2E-isomer of methoprene at C-2 but cannot rapidly isomerize the 2Z-isomer (Quistad et al., 1975d).

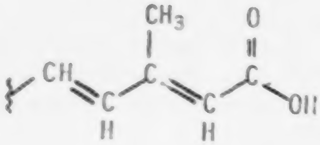
Esterases and oxidases prepared from homogenates of the house fly (Musca domestica L.), the flesh fly (Sarcophaga bullata) and blow fly (Phormia regina) also degraded juvenile hormone analogs of the altosid type. Except altosid itself, both esterases, present in all life stages, hydrolyzed all ester analogs tested to their respective acids. The microsomal oxidases metabolized all of the juvenile hormone analogs as well as altosid (Terriere and Yu, 1977; Yu and Terriere, 1975).



Altosid



11-hydroxy



1-Acid

11-hydroxy-Acid

Studies with housefly microsomal enzymes showed that the B-esterases present did not appreciably hydrolyze methoprene whereas other analogs were metabolized. Microsomal oxidase activity against juvenile hormone analogs was greater in resistant fly strains. Because not all of the analogs contained an O-methyl group but all did have the 2-4 double bond system, it is quite probable that oxidation occurred at one or both double bonds. (Oxidative attack at the Δ^4 double was shown in the previous article which showed formation of compound V.) (Yu and Terriere, 1975). Branched chain esters of methoprene analogs did not show significant difference in hydrolysis by housefly microsomal esterases. However, there was considerable difference in response to the analogs when bioassay studies were conducted during the pupal stage. At this period, microsomal activity is low compared to esterase activity. Methoprene was effective at 0.1 µg/pupa while others were ineffective at 10 µg/pupa. It was concluded that biological activity was determined by other factors (Yu and Terriere, 1977a).

Pupae of *Tenebrio molitor* and 5th-instar nymphs of *Oncopeltus fasciatus* were treated with altosid. In both insects, the expected metabolites were observed: 1-acid, 11-hydroxy, and 11-hydroxy-acid. Other metabolites were observed but not identified (Solomon and Metcalf, 1974).

In wheat, the half-life of methoprene was estimated to be 3 to 7 weeks, depending on moisture content. The only metabolite observed was the free acid (Rowlands, 1976).

Leaves of alfalfa and rice plants were treated with an emulsifiable concentrate of $[5\text{-}^{14}C]$methoprene. Leaves were removed and analyzed by use of chromatography and mass spectra. About 10 metabolites were observed in alfalfa but only 6 were identified. In rice, there were at least 13 metabolites. This is summarized in the following table (Quistad et al., 1974).

Methoprene Metabolites

Metabolite	Rice	Alfalfa
Compound II	+	+
Compound III		+
Compound IV	+	
Compound V		
Compound VI	+	+
Compound VII	+	
Conjugate III		+
Conjugate IV	+	+
Conjugate VI	+	+
Conjugate VII	+	+
Unextractable III conjugate		+
Unextractable VI conjugate	+	
[^{14}C]glucose	+	+
[^{14}C]Cellobiose	+	+
$^{14}CO_2$	+	+

The degradation of methoprene by unidentified pond microorganisms was studied. The half-life in the pond water was about 30 h at 0.001 ppm and 40 h at 0.01 ppm. At 0.42 ppm in pond water for 3 days, three primary metabolites were produced: hydroxy-ester (II); methoxy-acid (IV); hydroxy-acid (III). Some isomerization about the 2-ene bond occurred in each of these compounds as well as in methoprene itself. After 13 days incubation in pond water, the single major metabolite produced was identified as 7-methoxycitronellic acid (VI) (Schooley et al., 1975a).

In soil, [5-^{14}C]methoprene degradation was rapid. The half-life in sandy loam was calculated to be about 10 days. More than 50% of the applied dose was converted to $^{14}CO_2$. Humic acid, fulvic acid and humin fractions of the soil also contained radioactivity. The only primary metabolite observed was the hydroxy ester (II) (Schooley et al., 1975b).

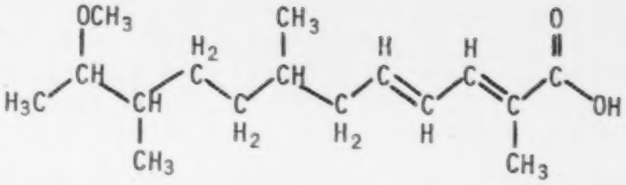
An aqueous emulsion of methoprene in pyrex was irradiated by sunlight for one week. Four compounds were identified:

3,7-dimethyl-7-methoxyoctanal(methoxycitronellal)
3,7-dimethyl-7-methoxyoctanoic acid
2,6-dimethyl-2-methoxynonan-8-one
4,5-epoxy-methoprene

About 46 other photoproducts were observed but not identified. When methoprene was exposed to sunlight as a thin film on glass through glass, 3% was isomerized to a 50:50 mixture of (2E,4E)- and (2Z,4E)-methoprene. In addition to about 50 unidentified products, the same four compounds previously observed were identified. In methanol, methoprene photolysis was very slow. After four days, a single major product was identified as isopropyl 2-hydroxyl-5-(2,6-dimethyl-6-methoxy)heptanyl dihydrofuran-2-carboxylate (Quistad et al., 1975b).

The stability of methoprene in water was studied. An emulsifiable concentrate persisted for 134 days at 4.5C and for 49 days at 20C in both fresh and salt water. The slow release flowable liquid degraded at 20C at about the same rate as did the E.C. formulation at 4.5C (Pree and Stewart, 1975).

ALTOSID Analogs



I

II=desmethoxy I

Microsomal esterases were prepared from insecticide-susceptible CSMA houseflies. This was incubated with branched chain esters of compounds I and II. *In vitro* hydrolysis was slower than with straight chain esters. Microsomal oxidases of the CSMA strain and of a resistant strain readily metabolized these analogs (Yu and Terriere, 1977a). Esterases and oxidases prepared from homogenates of the house fly (*Musca domestica* L.), the flesh fly (*Sarcophaga bullata*) and blow fly (*Phormia regina*) also degraded juvenile hormone analogs of the altosid type. Except altosid itself, both esterases, present in all life stages, hydrolyzed all ester analogs tested to their respective acids. The microsomal oxidases metabolized all of the juvenile hormone analogs as well as altosid (Terriere and Yu, 1977; Yu and Terriere, 1975).

ECDYSONE

In the midgut of *Manduca sexta* L., α-ecdysone was metabolized to the 20-hydroxy analog. This was catalyzed by a mitochondrial P-450 monooxygenese. This reaction was stimulated by citrate cycle compounds such as succinate, malate, and isocitrate and by NADPH, NADH, ATP and ADP (Mayer et al., 1978).

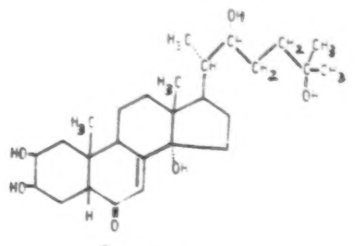
Most of the enzymes which convert α- and β-ecdysone to apolar compounds was found in the soluble fraction of housefly and flesh fly (*Sarcophaga bullata* Parker) homogenates. No activity was observed in any fractions from blow fly homogenates. Two enzymes were observed, one requiring NADPH and one not requiring NADPH. It was thought that 3-dehydro-ecdysone was formed from β-ecdysone by the latter system and that further transformation to the 3-α-hydroxy analog was effected by the NADPH-requiring enzyme (Yu and Terriere, 1977b).

The metabolism of α-ecdysone in larvae of *Tenebrio molitor* was investigated. Hydroxylation of α-ecdysone to β-ecdysone was very rapid. Dehydration and conjugation gave rise to other metabolites. Enzymatic cleavage of isolated material indicated the presence of sulfate, glucosiduronic, and β-glucosidic conjugates of 3-dehydroecdysteron, α-ecdysone and of two unidentified compounds (Weinheimer and Romer, 1977).

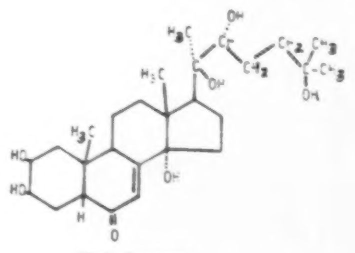
Different tissues of *Carcinus maenas* were incubated with ecdysone. Of five metabolites observed, one was identified as ecdysterone (Lachaise and Feyereisen, 1976). In two other species of crabs, *Pachygrapsus crassipes* and *Cancer antennarius*, the ability to hydroxylate α-ecdysone to β-ecdysone was concentrated in the mitochondria-enriched fraction of the testes (Chang and O'Connor, 1978).

The blowfly *Calliphora erythrocephala* converted β-ecdysone to 26-hydroxy-β-ecdysone (Greenwood and Russell, 1978). This compound has also been identified as a metabolite of the α-ecdysone analog 22,25-dideoxy-α-ecdysone in the tobacco hornworm *Manducca sexta* (Kaplanis et al., 1969; King, 1972; Kaplanis et al., 1972).

The flesh fly *Sarcophaga peregrina* rapidly metabolized injected β-ecdysone, forming conjugates in larvae and 3-epi-β-ecdysone in pupae (Moribayashi and Ohtaki, 1978).



α-Ecdysone



20-OH-Ecdysone

GOSSYPLURE [*Z*,*Z*- and *Z*,*E*-7,11-hexadecadien-1-ol acetate]

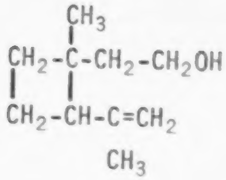
The half-life of gossyplure in soil at 32C was one day and in water 7 days. The major degradation product was identified as *Z*,*Z*- and *Z*,*E*-7,11-hexadecadienol. Leeching and photodegradation were not detected (Henson, 1977).

GRANDLURE

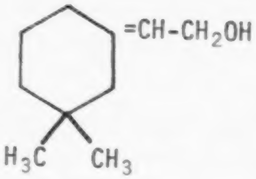
Grandlure is a four component pheromone consisting of:

I. cis-2-isopropenyl-1-methylcyclobutaneethanol;
II. (Z)-3,3-dimethyl-$\Delta^{1,\beta}$-cyclohexaneethanol;
III. (Z)-3,3-dimethyl-$\Delta^{1,\alpha}$-cyclohexaneacetaldehyde; and
IV. (E)-3,3-dimethyl-$\Delta^{1,\alpha}$-cyclohexaneacetaldehyde.

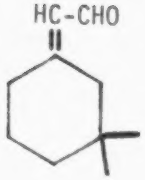
Analyses of solutions of compounds I and II indicated a high degree of stability. Compounds III and IV, however, were not stable. GC-MS was used to identify the products formed from III and IV as the respective acids (V and VI) and formate esters (VII and VIII) and an aldehyde (IX) that can form from either VII or VIII (Henson et al., 1976).



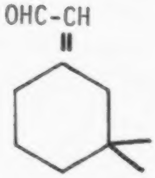
I



II



III

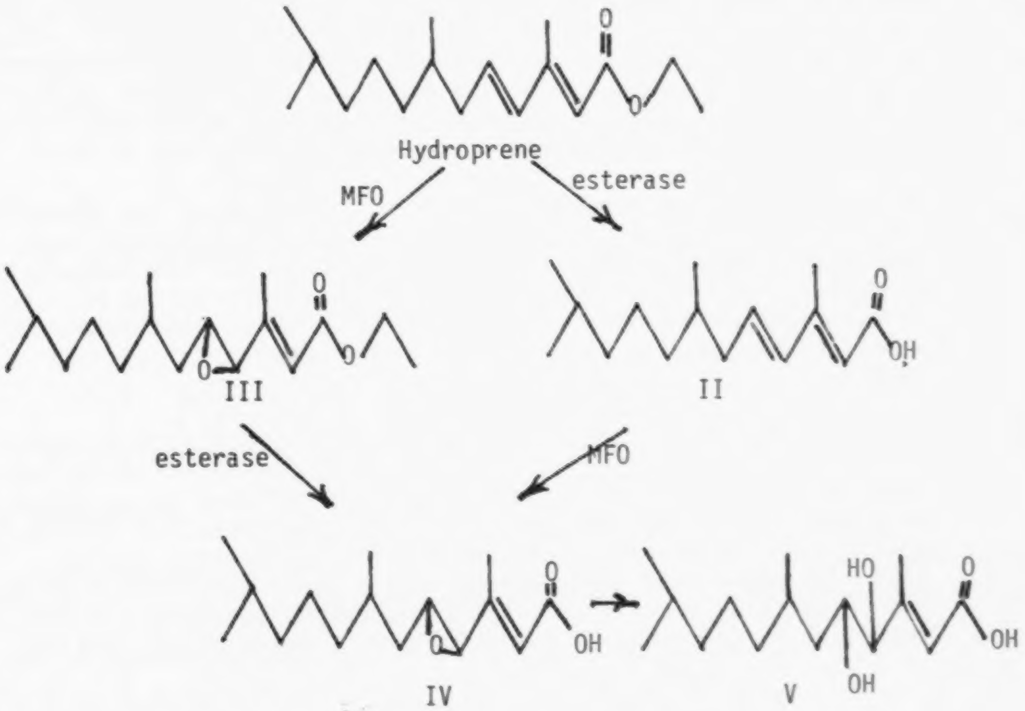


IV

HYDROPRENE [Ethyl 3,7,11-trimethyl-2,4-dodecadienoate]

Microsomal oxidases and esterases prepared from houseflies, flesh flies and blow flies produced the same metabolites. These have been identified as: the free acid (II); the epoxide (III); the epoxy-acid (IV); and the diol-acid (V). The position of the epoxy was not firmly established as 4,5 and may result from reaction of the 2,3-double bond. Some conjugated metabolites were observed but not identified. Part of these were converted to hydroprene acid by the use of sulfatase and β-glucosidase. Oxidative metabolism of hydroprene was increased fourfold by phenobarbital in the diet of adult houseflies. There was not effect on the activity of the esterase system (Yu and Terriere, 1977a).

House flies, flesh flies and blow flies, *in vivo* and *in vitro*, metabolized hydroprene. Two types of microsomal enzymes seemed to be involved *in vitro*. In the absence of NADPH, cochromatography in TLC and GLC systems showed the presence of the free acid, indicating an esterase activity. Inclusion of NADPH gave three more peaks. The data indicated these to be the 4,5 (or 2,3) hydroprene epoxide, the epoxy-acid and the diol-acid (Yu and Terriere, 1977b).



JH-1 (Cecropia JH-1) [*Trans,trans,cis*-methyl-10,11-epoxy-7-ethyl-3,11-dimethyl-2,6-tridecadienoate]

JH-1 was applied to the flour beetle, *Tribolium castaneum*. This hormone was rapidly metabolized by all stages tested. The main product of metabolism of this hormone was identified as the diol ester (II). Other metabolites identified were the acid (III) and acid-diol (IV) (Edwards and Rowland, 1977). *Locusta migratoria* also metabolized injected JH-1 to the diol, acid and diol-acid (Erley et al., 1975).

When the Colorado potato beetle was exposed to JH-1, similar results were observed. Degradation of injected exogenous hormone was very rapid and the $t_{1/2}$ was estimated to be 25 to 30 minutes (Kramer et al., 1977).

The metabolism of JH-I by grain weevils (*Sitophilus granarius*) was studied after topical application. In adult insecticide-susceptible and pyrethrin-resistant insects, the half-life was about 3 h and 2-1/2 h, respectively, and about 4 h in pupae. While both strains produced the same metabolites, the 1-acid was predominant in the susceptible strain whereas the acid-diol was the major metabolite in the resistant strain. Piperonyl butoxide delayed penetration and metabolism of JH-I and reduced production of the acid-diol in the resistant strain (Edwards and Rowlands, 1978).

After topical application of H-labeled JH-I to larvae and adult *Drosophila melanogaster*, analyses indicated the presence of the acid, diol, acid-diol and JH-I conjugates not further identified. No metabolism by *Drosophila* haemolymph was observed (Wilson and Gilbert, 1978).

Microsomes prepared from larvae, pupae, or adults of the house fly contained an esterase, an oxidase and an epoxide hydrase. The presence of NADPH in incubation mixtures increased the metabolism of JH-1. Identification of metabolites was not rigorous but the data indicated formation of the diol, acid, diepoxy acid, diepoxide, a tetrahydofuran diol (THF) and some unknown material (Yu and Terriere, 1978).

In vivo metabolism of JH-1 was compared in representative species of eight orders of insects. The major metabolites in all orders were the acid, acid-diol and conjugated metabolites believed to be glucosides or glucuronides. The diol was observed in these studies only in *T. molitor* and three species of lepidoptera: *Hyalophora cecropia*, *Antheraea pernyi* and *Samia cynthia*. Two other compounds were observed and tentatively identified from chromatographic evidence as the JH-tetrol in *H. cecropia*, *T. domestica* and *D. melanogaster* and the

JH-diepoxide in *D. melanogaster*. Those insects studied were: (N = larva; P = pupa; A = adult)

Thysanura
- *Thermobia domestica* (N)

Orthoptera
- *Periplaneta americana* (N)
- *Blattela germanica* (N)

Coleoptera
- *T. molitor* (P)
- *L. decemlineata* (P)
- *Hippodamia convergans* (N)

Hemiptera
- *Oncopeltus fasciatus* (N)
- *Pyrrhocoris apterus*

Diptera
- *Musca domestica* (P)
- *Drosophila melanogaster* (P)
- *C. americanus* (P)

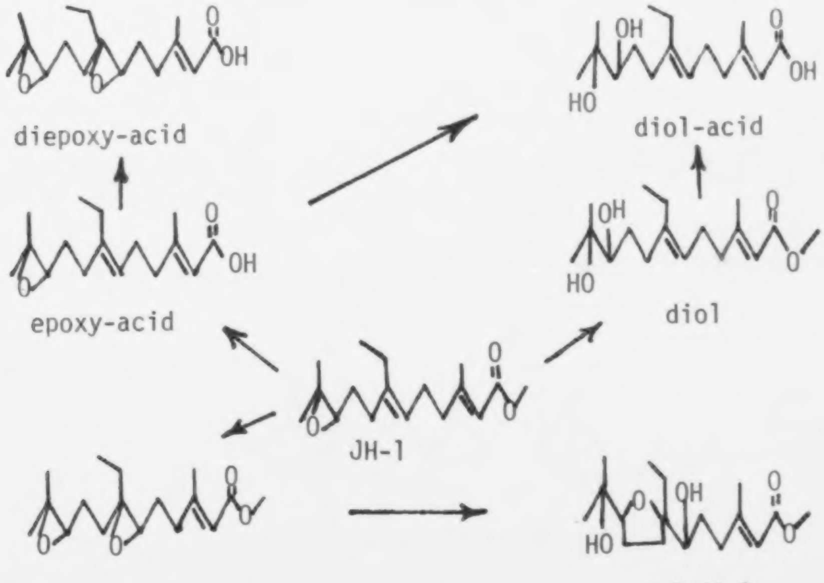
Hymenoptera
- *Apis mellifica* (A)
- *S. invicta* (P)
- *A. texana* (P)

Lepidoptera
- *Hyalophora cecropia* (P)
- *Antheraea pernyi* (P)
- *Samia cynthia* (P)
- *Manduca sexta* (P)

(Ajami and Riddiford, 1973)

In wing discs and fat body of tobacco hornworm (*Manduca sexta*) larvae, enzymes converted JH-1 to the acid, diol and acid-diol (Hammock et al., 1975).

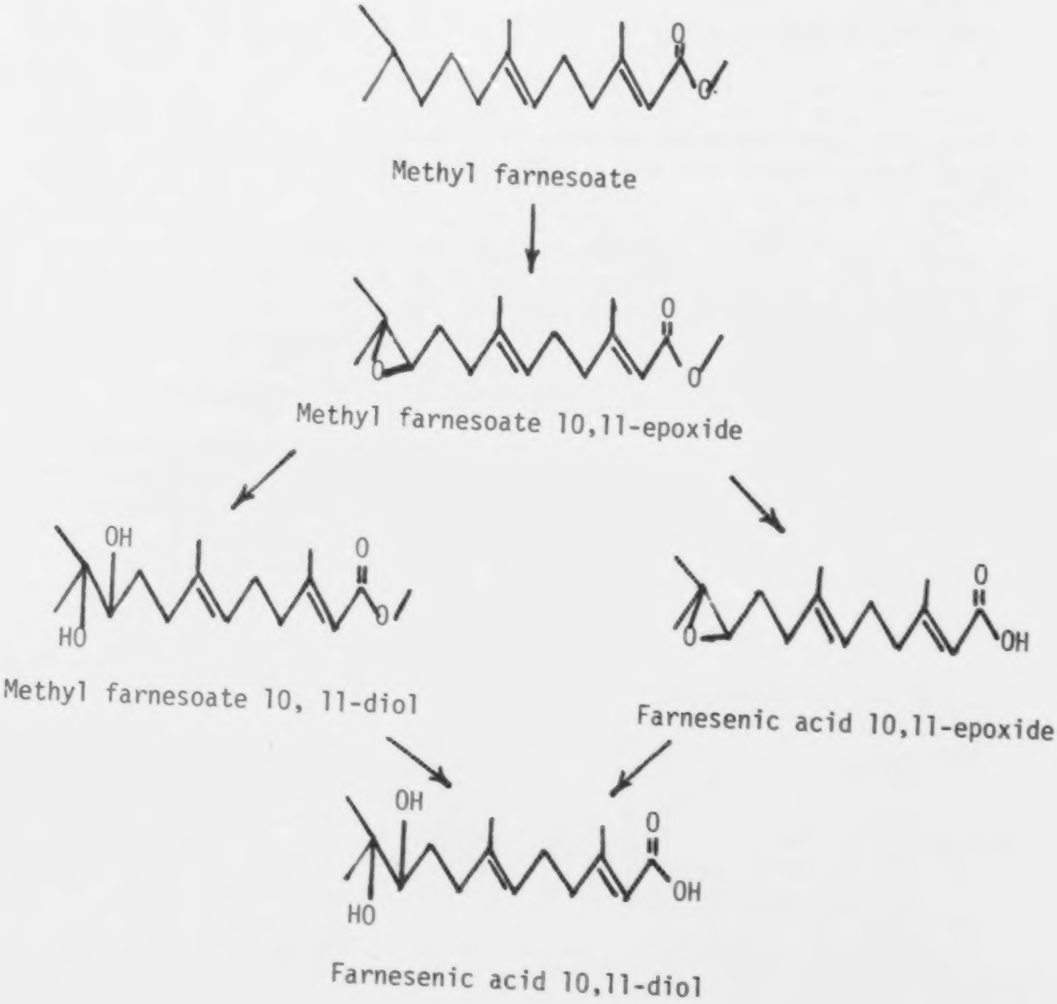
In wheat, JH-1 exhibited a half-life of 1 to 4 weeks, depending on moisture. The main metabolite was the free acid. The acid-diol was also present (Rowlands, 1976).



METHYL FARNESOATE [Methyl 3,7,11-trimethyl-*trans*-*trans*-dodeca-2,6-dienoate]

An NADPH-dependent system in corpus allatum homogenates from the cockroach *Blaberus giganteus* L. epoxidized methyl farnesoate to the 10,11-epoxide (Hammock and Mumby, 1978).

Labeled methyl farnesoate 10,11-epoxide was injected into 5th instar of *Rhodnius prolixus* and *Schistocerca gregaria*. Twenty hours later ether extracts were examined by TLC. In addition to unchanged material, farnesenic acid 10,11-epoxide, farnesenic acid 10,11-diol and methyl farnesoate 10,11-diol were observed and confirmed by GLC of the TMS ethers. In *Schistocerca* whole insect, the foregoing metabolites were present as water soluble conjugates, primarily as glucosides (White, 1972).


O
O
Methyl farnesoate
O
O
O
Methyl farnesoate 10,11-epoxide
OH
O
HO
O
Methyl farnesoate 10, 11-diol
O
O
OH
Farnesenic acid 10,11-epoxide
OH
O
HO
OH
Farnesenic acid 10,11-diol

PRECOCENE II [6,7-Dimethoxy-2,2-dimethylchromene]

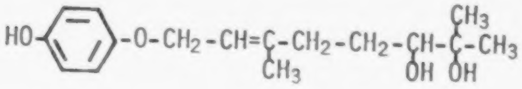
Nine insect species were treated with precocene II. These included cabbage looper (*Trichoplusia nil*), European corn looper (*Ostrinia nubilalis*), European chafer grub (*Amphimallon majalis*), milkweed bug (*Oncopeltus fasciatus*), cotton stainer (*Dysdercus cingulatus*), hide beetle (*Dermestes maculatus*), yellow mealworm (*Tenebrio molitor*), navel orangeworm (*Paramyelois transitella*) and wax moth (*Galleria mellonella*). In each case, the main metabolite was 6,7-dimethoxy-2,2-dimethylchroman-3,4-diol. Two other metabolites were identified as 6,7-dimethoxy-2,2-dimethylchroman-3-ol, 3,4-epoxy-6,7-dimethoxy-2,2-dimethylchroman. *In vivo* studies with European corn borer gut and tissue body tissue homogenates indicated that an MFO system catalyzed the metabolism (Ohta et al., 1977).

R-20458 (Phenyl epoxygeranyl ether, Ethyl-epoxide) [1-(4'-Ethyl phenoxy)-3,7-dimethyl-6,7-epoxy-*trans*-2-octene]

R-20458 was orally administered to rats. Urine and feces was collected and analyzed. Chromatography, GC-MS and NMR were used to identify metabolites. In urine, compounds I-XIV were observed and compounds XV-XXV in feces. Several metabolites were not completely characterized (Table I) (Hoffman et al., 1973).

Table I.

I.



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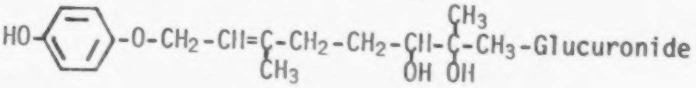

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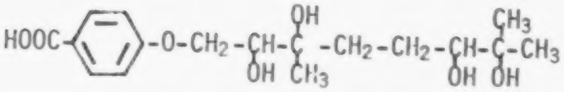

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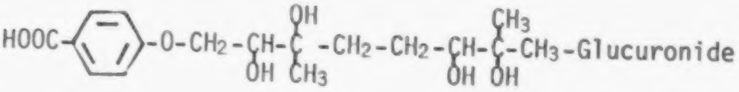

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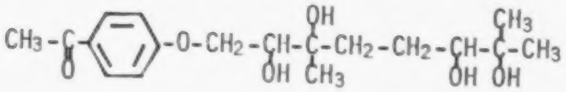

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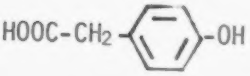

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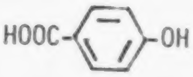

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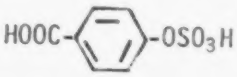

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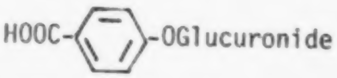
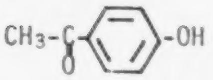


X. 2,6,7-$(OH)_3$-1-(4'-acetylphenoxy)-analog

XI. 3,6,7-$(OH)_3$-1-(4'-acetylphenoxy)-analog

XII.



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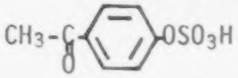

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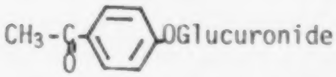

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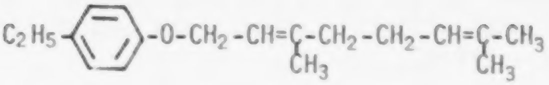

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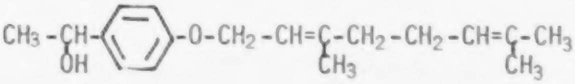

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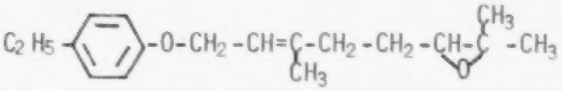

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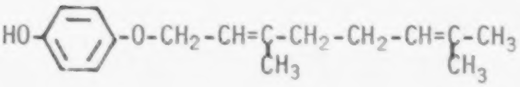

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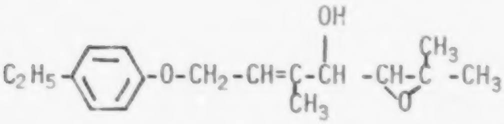
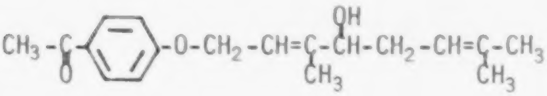
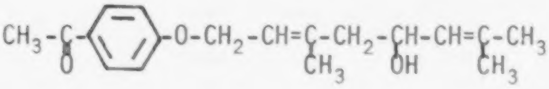


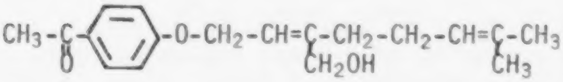
XX.



XXI.



XXII.



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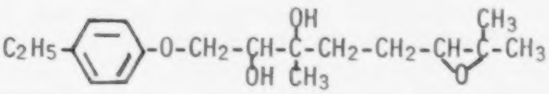
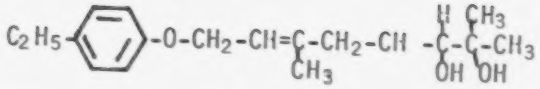
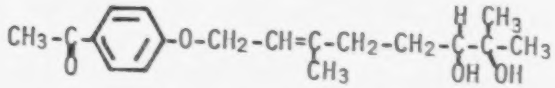


XXIV. 

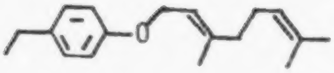
XXV. 

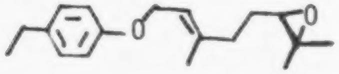
Radioactive R-20458 was injected into cockroaches (*Periplaneta americana*). Analyses of methanol extracts contained the ethyl-diol as the major identified metabolite, based on cochromatography and derivatization. A compound thought to be the ethyl-tetraol was also observed. Results of studies with five insects are summarized (Tabel II) (Hammock et al., 1974).

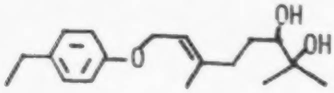
Table II.

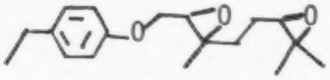
Metabolite	Insect *M. domestica*	*S. bullata*	*M. sexta*	*T. molitor*	*P. americana*
α-Hydroxyethyl-diene	tr		tr		+
β-Hydroxyethyl-diene			+		+
Aceto-diene		+	+		+
Olefinic primary alcohol	+				
Olefinic aldehyde	+				
Olefinic carboxylic acid	+++				
Hydroxylated olefinic carboxylic acid	+				
α-Hydroxyethyl-epoxide	+++	+	+		+
β-Hydroxyethyl-epoxide			+		+
Aceto-epoxide	++	++++	+		+
Ethyl-diol	++	+	++++	++++	++++
α-Hydroxyethvl-diol	+++	+	+		+
β-Hydroxyethyl-diol	+				
Aceto-diol	+	+	+		+
Ethyl-*cis*-thf-diol	+	+	+		+
Ethyl-*trans*-thf-diol			+		+
Ethyl-diepoxide	+		+		+
Ethyl-thp-diols I&II	tr	tr	tr		tr

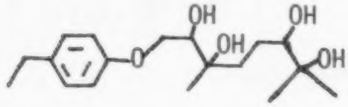
R-20458-^{14}C was administered orally and dermally to steers. After oral administration, urinary excretion of ^{14}C was the major route of elimination with 85% of the dose excreted in 7 days. Ethyl phenol and acetophenol were the major metabolites observed in urine but most of these compounds were present as glucuronide and/or sulfate conjugates. Two others were identified as ethyl diol and aceto diol. About 13 other compounds were observed but not identified. A fecal metabolite

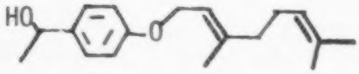
I.  ethyl diene

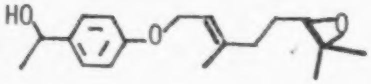
II.  ethyl epoxide

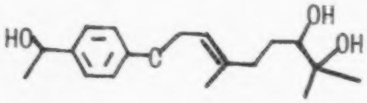
III.  ethyl diol

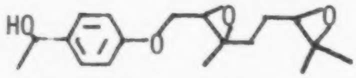
IV.  ethyl diepoxide

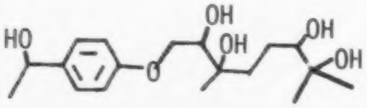
V.  ethyl tetraol

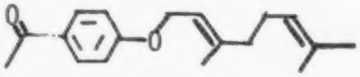
VI.  α-hydroxyethyl diene

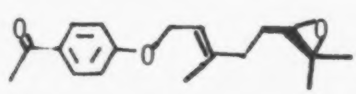
VII.  α-hydroxyethyl epoxide

VIII.  α-hydroxyethyl diol

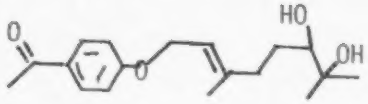
IX.  α-hydroxyethyl diepoxide

X.  α-hydroxyethyl tetraol

XI.  aceto diene

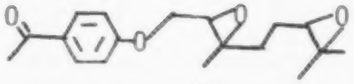
XII.  aceto epoxide

XIII.



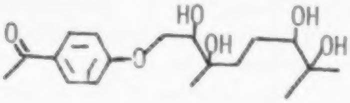
aceto diol

XIV.



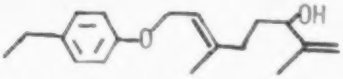
aceto diepoxide

XV.



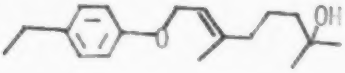
aceto tetraol

XVI.



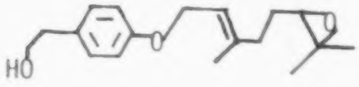
ethyl 6-hydroxy-2,7-diene

XVII.



ethyl 6-hydroxy-2-ene

XVIII.



β-hydroxyethyl epoxide

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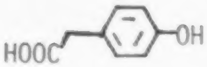
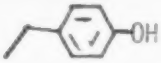


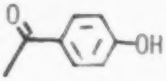
4-hydroxyphenylacetic acid

XX.



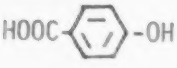
4-ethylphenol

XXI.



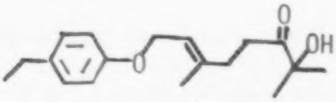
4-acetophenol

XXII.



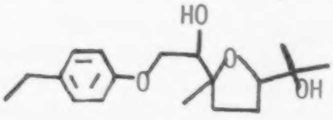
4-hydroxybenzoic acid

XXIII.



ethyl α-hydroxyketone

XXIV.

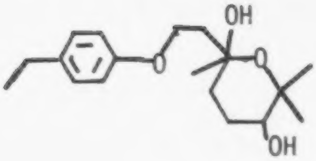


cis-ethyl-thf-diol

XXV.

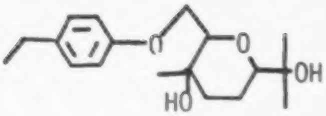
trans-ethyl-thf-diol

XXVI.



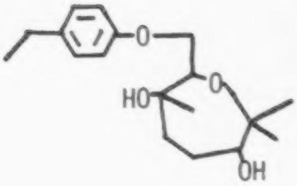
ethyl-thp-diol I

XXVII.



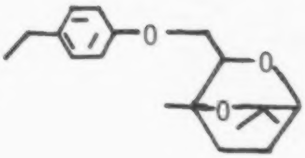
ethyl-thp-diol II

XXVIII.



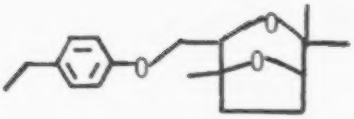
ethyloxepane diol

XXIX.



ethyl bicyclic ether I

XXX.



ethyl bicyclic ether II

was identified as the ethyldiene by means of NMR and GLC-MS. Treatment of the compound with *m*-chloroperoxybenzoic acid regenerated the epoxide R-20458. The diene was also formed by incubation of the epoxide with ovine digestive tract fluids. Another was not identified. Methanol extracts of treated hair and skin contained the ethyldiene, ethylphenol, ethyldiol, and ethyl-6-hydroxy-2,7-diene (Ivie, 1976; Ivie et al., 1976b).

R-20458 labeled in the phenyl ring with ^{14}C was orally administered to mice and ^{3}H-phenyl was administered i.p. in rats. Almost all of the radioactivity appeared in the urine and feces within 96 h. About 34% of the dose was excreted as conjugates. Metabolism and phytolysis of R-20458 and the related ethyl-diene are summarized in the following tables (Gill et al., 1974).

I	Ethyl-diene
II	Ethyl-epoxide
III	Ethyl-diol
IV	Ethyl-diepoxide
V	Ethyl-tetraol
VI	α-Hydroxyethyl-diene
VII	α-Hydroxyethyl-epoxide
VIII	α-Hydroxyethyl-diol
IX	α-Hydroxyethyl-diepoxide
X	α-Hydroxyethyl-tetraol
XI	Aceto-diene
XII	Aceto-epoxide
XIII	Aceto-diol
XIV	Aceto-diepoxide
XV	Aceto-tetraol
XVI	Ethyl-6-hydroxy-2,7-diene
XVII	Ethyl-6-hydroxy-2-ene
XVIII	β-Hydroxyethyl-epoxide
XIX	4-Hydroxyphenylacetic acid
XX	4-Ethylphenol
XXI	4-Acetophenol
XXII	4-Hydroxybenzoic acid
XXIII	Ethyl α-hydroxyketone
XXIV	*Cis*-ethyl-thf-diol
XXV	*Trans*-ethyl-thf-diol
XXVI	Ethyl-thp-diol I
XXVII	Ethyl-thp-diol II
XXVIII	Ethyl-oxepane-diol
XXIX	Ethyl-bicyclic ethers I
XXX	Ethyl-bicyclic ethers II

Degradation of ethyldiene, ethyl epoxide and ethyldiol

Metabolite	Rat, mouse, rabbit liver microsomes + NADPH	*In vivo* Mice		Rat & Mouse liver microsomes + NADPH	Mouse liver microsomes + NADPH	Rat liver microsomes + NADPH			Algae								
		Urine	Feces						Chlamydomonas			Chlorella			Chlorophyll		
I				*					*			*			*		
II	*	*	*	+					+	*			*			*	
III	+		+	+	*				+	+		+	+	*	+	+	*
IV	+					*			+	+					+	+	
V											*						
VI				+					+								
VII	+			+				*									
VIII	+				+			+	+	+	+		+	+			+
IX	+					+											
X																	
XI				+					+								
XII	+						*	+									
XIII	+		+		+		+	+									
XIV	+																
XV		+															
XVI																	
XVII																	
XVIII	+																
XIX		+	+														
XX		+		+					+	+							+
XXI		+	+	+					+	+	+	+			+	+	+
XXII		+															
XXIII					+												
XXIV	+				+	+			+	+	+			+			+
XXV	+				+	+			+	+	+			+			+
XXVI						+											
XXVII					+	+											
XXVIII						+											
XXIX	+					+											
XXX	+					+											

* Starting compound

Photolysis of ethyldiene, ethyl epoxide, ethyl diepoxide and ethyldiol by sunlight (4 h)

	On Silica Gel				In Water		
	Ethyl-diene	Ethyl-epox.	Ethyl-diol	Ethyl-diepox.	Ethyl-diene	Ethyl-epox.	Ethyl-diol
I	*				*		
II	+	*			+	*	
III		+	*		+	+	*
IV	+	+		*	+	+	
V							
VI							
VII						+	
VIII						+	+
IX				+			
X							
XI							
XII						+	
XIII						+	+
XIV				+			
XV							
XVI					+		
XVII	+						
XVIII							
XIX							
XX		+	+		+	+	
XXI		+	+		+	+	+
XXII							
XXIII		+	+				
XXIV		+	+	+	+	+	+
XXV		+	+	+	+	+	+
XXVI		+		+	+		
XXVII		+		+	+		
XXVIII				+			
XXIX		+		+			
XXX		+		+			

* Starting compound.

R-20458 was administered to the imported fire ant (*Solenopsis invicta*). The $t_{1/2}$ never exceeded 2 days (Wendel, 1977). The main free metabolites in adults and larvae were ethyl-diol and aceto-epoxide. Extremely polar materials, conjugates, were also present in larger amounts (Wendel and Vinson, 1978).

Six hours after application to houseflies, in addition to starting material, only trace amounts of the ethyl-*t*-alcohol was observed after exposure to the ethyl alkoxides and ethyl-diol after exposure to the ethyl epoxide. The stable fly (*Stomoxys calcitrans* L.) produced ethyl-*t*-alcohol from the alkoxides. When the ethyl-epxoide was applied, in addition to unidentified metabolites there was some ethyl-diol, α-hydroxyethyl epoxide, aceto epoxide, ethyl diepoxide, and α-hydroxyethyl diol. In mealworms (*Tenebrio molitor* L.) *O*-dealkylation gave the ethyl-*t*-alcohol from the ethyl alkoxide and ethyl diol from the ethyl epxoide (Hammock et al., 1975).

Enzyme studies were conducted with mouse liver microsomes-NADPH and housefly microsome-NADPH systems. Results are summarized in the following table (Hammock et al., 1975).

	Housefly	Mouse	
ethyl alkoxide	*	*	
ethyl epoxide		+	*
ethyl diol			+
ethyl diepoxide			+
ethyl *t*-alcohol	+	+	
α-hydroxyethyl-*t*-alcohol	+	+	
aceto alkoxide	+		+
α-hydroxyethyl alkoxide	+	+	
α-hydroxyethyl epoxide			+
α-hydroxyethyl diol			+

*Starting compounds

Little photodecomposition of the ethyl epoxide or the ethyl alkoxides occurs on silica gel in the dark. When exposed to a sunlamp, 25% decomposition to unidentified compounds occurred in 7.8 to 11.4 h (Hammock et al., 1975).